The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 136, No. 2 — CHICAGO, ILLINOIS — JANUARY 10, 1948

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BCG VACCINATION IN ALL AGE GROUPS

Methods and Results of a Strictly Controlled Study

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A radical change in our thinking in regard to BCG vaccination has been initiated by the United States Public Health Service under the guidance of Dr. Herman E. Hilleboe, one time Assistant Surgeon General, with the approval of Surgeon General Thomas Parran. Under the auspices of the United States Public Health Service, a conference on BCG was held in Washington on Sept. 7, 1946.[1] This representative body, composed of proponents and opponents of BCG vaccination, concluded and recommended essentially as follows:

"A. Medical literature fails to reveal any proven cases of progressive disease as a result of BCG vaccination.

B. From studies presented at the conference, it appears that BCG vaccination confers increased resistance to tuberculosis for the limited period of time covered in these studies.

C. Extensive investigations should be carried on cooperatively with recognized research groups throughout the country during the coming years, especially in population groups highly exposed to tuberculous infection.

D. It was recommended tha a single laboratory be established by the Tuberculosis Control Division to produce BCG vaccine for the whole country for use in research programs proposed at this conference.

BCG (Bacillus of Calmette and Guérin) is a nonvirulent bovine tubercle bacillus originally isolated from the milk of a tuberculous cow in 1906. The virulence of this organism was then reduced by the regular transfers on a bile potato medium over a period of thirteen years. The avirulent organism was able to produce local nodular lesions in animals, but there was no evidence of progression or generalization of the process. It was then discovered that these animals when infected with virulent tubercle bacilli resisted a progressive infection to a great extent. With the assurance that the organism was harmless and that it afforded a certain degree of protection against virulent tubercle bacilli,[2] human application was instigated in 1921 by Weill-Hallé in Paris.[3] Since that time it is estimated that some ten million vaccinations have been performed throughout the world.

The reluctance to accept BCG in the United States stems largely from the laboratory studies of Petroff and the tragedy in Lübeck, Germany. Petroff and his co-workers[4] dissociated BCG into rough "R" and smooth "S" forms. The latter, it was claimed, had the ability at times to produce progressive disease in animals.[5] One of us (S. R. R.), working in an isolated laboratory where only BCG was cultured, using many thousands of cultures and animals over a period of thirteen years, has been able to dissociate BCG but has never seen progressive disease following BCG inoculation in any phase.[6] As much as three hundred thousand times the human dose, calculated by weight, has been injected into animals without deleterious effect.[7] Petroff, in a personal communication in 1934, conceded at that time that BCG was probably a pure "R" form and as such incapable of producing progressive tuberculosis.

The disaster that occurred in Lübeck, Germany, was one in which 271 infants received what was supposed to have been BCG vaccine by mouth. Seventy-seven died of progressive disease following ingestion of this mixture. It was later proved by the Robert Koch Institute of Berlin for the German government that the vaccine used was a mixture of BCG and a virulent strain of tubercle bacilli which was kept in the same incubator as BCG. The virulent strain in question was received from the nearby town of Kiel, and was readily identified by its peculiar characteristic of producing a phosphorescent green color in Sauton medium. For this act of malpractice, those responsible were imprisoned.[8]

The following study has been in continuous operation for thirteen years and constitutes the longest continu-

From Tice Laboratory and Clinic of the Chicago Municipal Tuberculosis Sanitarium and the University of Illinois College of Medicine.

1. Report of a Conference on BCG Vaccination, Pub. Health Rep. **62**: 346-350, 1947.

2. Calmette, A.; Guérin, C.; Boquet, A., and Nègre, L.: La vaccination préventive contre la tuberculose par le BCG, Paris, Masson & Cie, 1927.

3. Weill-Hallé, B., and Turpin, R.: Premiers essais de vaccination antituberculeuse de l'enfant par le bacille Calmette-Guérin (BCG), Bull. et mém. Soc. méd. d. hôp. de Paris **49**: 1589-1601, 1925.

4. Petroff, S. A.; Branch, A., and Steenken, W., Jr.: Study of Bacillus-Calmette-Guérin (BCG): Biological Characteristics, Cultural "Dissociation" and Animal Experimentation, Am. Rev. Tuberc. **19**: 9-46, 1929.

5. Petroff.[4] Sasano, K. T., and Mediar, E. M.: Studies of Bacillus-Calmette-Guérin Strain of Tubercle Bacillus; Effect "in Vitro" of Environment on Virulence of BCG, Am. Rev. Tuberc. **23**: 215-222, 1931. Reed, G. B.; Orr, J. H., and Rice, C. E.: Studies in Variability of Tubercle Bacilli: BCG, Canad. J. Research **11**: 362-377, 1934. Dreyer, G., and Vollum, R. L.: Mutation and Pathogenicity Experiments with BCG, Lancet **1**: 9-15, 1931.

6. Rosenthal, S. R.: The General Tissue and Humoral Response to an Avirulent Tubercle Bacillus, Urbana, University of Illinois Press, 1938. Boquet, A., and Nègre, L.: Sur la fixité des caractères d'atténuation de la virulence du vaccin BCG, Compt. rend. Soc. de biol. **103**: 290-292, 1930. Kraus, R.: Ueber die Dissoziation des BCG—Stammes nach Petroff, Ztschr. f. Immunitätsforsch. u. exper. Therap. **61**: 454-459, 1929. Birkhaug, K. E.: Études sur la dissociation du Mycobacterium tuberculosis, Ann. Inst. Pasteur **54**: 19-70 and 195-244, 1935.

7. Rosenthal, S. R.; Blahd, M., and Leslie, E. I.: Ten Years' Experience with BCG (Experimental and Clinical), J. Pediat. **26**: 470-480, 1945.

8. Lange, L., and Pescatore, H.: Die Säuglingstuberkulose in Lübeck, Berlin, Julius Springer, 1935.

ous experiment in the United States. The first three years were spent entirely on research in animals, and during the last ten years human beings of every age group have been vaccinated. This study is unique in that: (1) the controls represent a population similar to the vaccinated, and (2) the principle of isolating the vaccinated person until the tuberculin test became positive in result was practiced when tuberculosis was present in the household. In the latter group, controls were isolated for similar periods of time. The major premise of this study was that BCG should supplement present methods of early diagnosis and segregation.

GROUPS STUDIED

1. *Newborn Infants Delivered at the Cook County Hospital of Chicago.*—Arrangements were made with the mothers in the prenatal clinic so that enough time was available to examine roentgenologically each member of the household. The children in this group came from households in which there was no known tuberculosis as demonstrated by roentgen examination of each member. The infants were vaccinated or accepted as controls before they left the hospital, and no isolation was practiced. This study has been in progress for ten years.

2. *Infants Born of Tuberculous Parents Anywhere in Chicago.*—Isolation of the infants was practiced for the controls and vaccinated alike, usually from six to twelve weeks, depending on the severity of the disease. Children were returned to their families only if examinations of concentrated sputum of the tuberculous member, within six months, were negative in result. This group has been followed for seven years.

3. *Student Nurses at the Cook County Hospital* (With Drs. Rhodes and Afremow).—Students were tuberculin tested and vaccinated during their first week in training. They were not allowed to go onto ward for at least one month after vaccination. This study has been in progress for seven years.

4. *Medical Students at the University of Illinois.*—These students were examined roentgenologically and tuberculin tested at the end of their first year or the beginning of their second year. The negative reactors who desired vaccination were vaccinated. Those who refused vaccination were used for the control group. This group was begun seven years ago.

5. *Children in a Federal Housing Project.*—The entire community was first examined roentgenologically and those with active pulmonary disease were isolated. Alternate children up to 10 years of age who did not react to tuberculin were vaccinated. This study is now in its sixth year.

6. *Inmates of a Mental Institution.*—After a roentgen survey and tuberculin testing, the persons with active disease were isolated. Seven months later the negative reactors were again tested. Alternate negative reactors were vaccinated. All age groups were included. This study was initiated four years ago.

The ensuing report embraces for the main part groups 1 and 2. Groups 3 to 6 are only mentioned, as some of the final results are not available, and they will be published in detail elsewhere.

THE VACCINE

The cultures used for the vaccine are transfers from the original culture at the Pasteur Institute in Paris. These were brought over by one of us (S. R. R.) in March of 1934 and have been transferred continuously every two weeks since that time. For each batch of vaccine, virulence studies are made in animals. The reactions in animals and the growth characteristics of this organism have not appreciably altered during this thirteen year period. The type of lesion produced in animals and the rapidity of development of a tuberculin action in animal and man remain the same. The vaccine is gathered from the growth on synthetic mediums (Sauton) and is a suspension of bacilli in a buffered salt solution. The vaccine is put up in capillary tubes in much the same way as is done for vaccinia.

METHOD OF APPLICATION

The oral method of administration originally advocated by Calmette and used by Weill-Hallé [8] was largely replaced by the intracutaneous route suggested by Wallgren.[9] The former method yielded a small percentage of reactors to tuberculin, while the latter yielded a high percentage. However, the local sequelae following the intracutaneous method were: ulcerations which may persist for months, focal abscesses and suppuration of lymph nodes. In a recent report from Denmark by Holm [10] universal ulceration was reported following intracutaneous vaccination. In 26 of 3,369 vaccinations, local abscesses or suppurated lymph nodes developed. Residual scars were the rule. A similar experience was reported in the study with Indians in this country by Aronson.[11] It is obvious that it would facilitate the generalized use of a vaccination if complications could be eliminated. To this end one of us (S. R. R.) described the scarification method of multiple punctures.[12] In thousands of vaccinations by this method complications have been practically nil. The actual technic is as follows:

A drop of vaccine is placed on the outer aspect of the alcohol-cleansed arm. A sewing type needle, similar to the one used for vaccinia, is held between the thumb and the index finger about 1.5 cm. from the point. The thumb and needle should form a continuous line. With the shaft of the needle held tangentially to the skin, the vaccine is spread in linear fashion for a distance of 2.5 cm. By a downward pressure, exerted to a large extent by the thumb, the skin is pierced with the needle point through the vaccine. Following this downstroke, which engages the point of the needle into the skin, an upward movement is exercised without disengaging the needle. The point of the needle remains buried in the skin on the upstroke. This precaution makes the method foolproof. The punctures are placed about 2 to 4 mm. apart, and ten punctures are made in a line. The vaccine is spread to the second line parallel to the first and 4 to 6 mm. away. Thus three lines of ten punctures each are made in an area of approximately 2.5 by 1.5 cm. The vaccine is allowed to dry on the arm; no blotting or covering with dressings is practiced. Wetting of the arm should be avoided for twenty-four hours.

The lesions following the multiple puncture method in newborn infants resembles goose flesh after two to six weeks following vaccination. The mother rarely knows which arm was inoculated. In children and adults each puncture progresses to form pink papules from a pinhead to 3 mm. in size. These papules after four to eight weeks regress rapidly. The recipient is

9. Wallgren, A.: Intradermal Vaccinations with BCG Virus: Preliminary Note, J. A. M. A. **91:** 1876-1881 (Dec. 15) 1928.
10. Holm, J.: BCG Vaccination in Denmark, Pub. Health Rep. **61:** 1298-1315, 1946.
11. Aronson, J. D.; Parr, E. L., and Saylor, R. M.: BCG Vaccine: Its Preparation and Local Reaction to Its Injection, Am. Rev. Tuberc. **42:** 651-666, 1940.
12. Rosenthal, S. R.: The Multiple Puncture Method of BCG Vaccination, Am. Rev. Tuberc. **39:** 128-134, 1939.

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usually unaware of which arm was scarified. The draining lymph nodes may be palpable two weeks after vaccination, but never enlarge to the extent that the recipient is aware of it. Ulceration and breaking down of lymph nodes have never been seen.

In a special study made to determine how soon the tuberculin reaction becomes positive after vaccination at birth, it was found that none reacted before ten days (37 cases). Out of 57 tested at eleven to thirteen days, 8, or 14 per cent, reacted; of 30 tested at twenty-three to thirty-one days, 29, or 96.6 per cent, had positive reactions and of 53 tested at thirty-two to fifty-four days, 51, or 98.1 per cent, reacted positively. In young adults 50 per cent react to 1 mg. of old tuberculin in one week and 90 per cent in two weeks. Table 1 gives the results of tuberculin reaction in children, all vaccinated on the third to seventh day of life. The Vollmer patch test was done in these cases and, if negative in result, was followed by the Mantoux test, 1 mg. of old tuberculin being used. As the table shows, the tuberculin reactions continue to be positive in over 90 per cent of the cases up to four years and in about 80

TABLE 1.—*Tuberculin Reactions Following a Single Vaccination in the Noncontact Group*

Age	Number Registered	Number Tested	Number Positive	Percentage Positive
0-3 mo.	1,417	1,345	1,341	99.70
4-7 mo.	1,385	1,299	1,294	99.61
8-12 mo.	1,362	1,249	1,244	99.60
1-1½ yr.	1,318	1,196	1,187	99.26
1½-2 yr.	1,271	1,125	1,109	98.58
2-2½ yr.	1,231	1,059	1,037	97.92
2½-3 yr.	1,176	990	949	95.86
3-3½ yr.	1,112	908	868	95.59
3½-4 yr.	1,065	852	789	92.61
4-4½ yr.	932	765	688	89.93
4½-5 yr.	911	680	600	88.23
5-5½ yr.	811	587	504	85.86
5½-6 yr.	700	484	399	82.44
6-6½ yr.	606	407	325	79.85
6½-7 yr.	496	321	247	76.95
7-7½ yr.	359	228	165	72.37
7½-8 yr.	247	148	108	72.97
8-8½ yr.	158	94	60	63.83
8½-9 yr.	93	53	25	47.17
9-9½ yr.	36	20	12	60.00

per cent after six to six and a half years following a single vaccination. These results are equal or superior to those obtained when other methods of introducing the vaccine are used. This has been verified by Nègre and Bretey [13] and Weill-Hallé [14] of France, Birkhaug of Norway,[15] Wallgren of Sweden,[16] and Etcheverry,[17] Gines and Rebull Richieri of Uruguay.[18]

For comparison, table 2 lists the controls for this group. It will be noted that there is a high rate of tuberculin reaction conversion. This is not surprising in that children included in this part of the study come from the poorest districts of Chicago, where the tuberculosis death rate is high. The high tuberculin reaction conversion of the controls is of special interest in that members of the household of these children had normal roentgenograms of the chest. This indicates the high incidence of casual infection and the degree of exposure for the vaccinated and the control groups.

In older children and adults the duration of tuberculin reactions following a single vaccination was similar as far as they were tested (88.6 per cent of the 35 nurses tested reacted after three years).

TABLE 2.—*Tuberculin Reactions in the Noncontact Control Group*

Age	Number Registered	Number Tested	Number Positive	Percentage Positive
0-3 mo.	1,414	1,344	3	0.22
4-7 mo.	1,380	1,305	13	0.99
8-12mo.	1,308	1,279	52	4.06
1-1½ yr.	1,248	1,234	100	8.10
1½-2 yr.	1,324	1,193	149	12.49
2-2½ yr.	1,291	1,145	194	16.94
2½-3 yr.	1,252	1,084	226	20.85
3-3½ yr.	1,188	1,008	243	24.10
3½-4 yr.	1,136	950	255	26.84
4-4½ yr.	1,048	865	240	27.75
4½-5 yr.	959	781	233	29.83
5-5½ yr.	853	679	213	31.37
5½-6 yr.	756	569	187	32.86
6-6½ yr.	616	439	156	35.53
6½-7 yr.	495	351	135	38.46
7-7½ yr.	364	249	102	40.96
7½-8 yr.	245	165	69	41.82
8-8½ yr.	161	109	49	44.95
8½-9 yr.	79	47	25	53.19
9-9½ yr.	30	17	12	70.59

EFFICACY OF THE VACCINATION, GROUP I

There was but 1 person who was hospitalized for tuberculosis in the vaccinated group compared with 15 for the controls. Considering roentgen evidence of disease such as parenchymal infiltration, hilar infiltration and calcification, there were 11 cases in the vaccinated and 39 in the control group. There was 1 death in the vaccinated as compared with 7 in the control group (table 3).

The clinical course and the postmortem findings of the vaccinated child that died revealed progressive primary tuberculosis in the lung and tuberculous meningitis. There were no lesions at the site of BCG inoculation or in the draining lymph nodes. It is noteworthy that six months after vaccination this child failed to react to the first Vollmer patch test and had only a weakly positive reaction on retesting. At fifteen months the patch test again elicited a negative reaction and at eighteen months a weakly positive reaction. In a reconstruction of this case, it can be considered as one which

TABLE 3.—*Incidence of Tuberculosis in Children Followed Since Birth*

	Noncontact		Contact	
	Vaccinated	Controls	Vaccinated	Controls
Total number of children	1,417	1,414	151	105
Person-years observed	5,627	6,032	517	284
Cases of tuberculosis				
Total number	11	39	2	5
Rate *	1.95	6.46	3.86	17.60
Cases hospitalized				
Number	1	15	1	5
Rate *	0.17	2.48	1.93	17.60
Deaths from tuberculosis				
Number	1	7	0	4
Rate *	0.17	1.16	0	14.09
Deaths from other causes				
Number	27†	22†	3†	2†
Rate *	4.79	3.65	5.79	7.04

* Rate per thousand person-years' observation.
† In 42 of the 54 deaths, or 77.7 per cent, autopsies or coroner's examination verified the cause of death.

13. Nègre, L., and Bretey, J.: Vaccination par le BCG par scarifications cutanées, Paris, Masson & Cie, 1942.
14. Weill-Hallé, B., and Lagroua, M. A.: La vaccination contre la tuberculose par le BCG: Méthode des scarifications cutanées, Paris, Gaston Doin & Cie, 1942.
15. Birkhaug, K.: Protective Value of Intracutaneous and Percutaneous Methods of BCG Vaccination (Comparative Experimental Investigation), Acta med. Scandinav. **117**: 274-312, 1944.
16. Wallgren, A.: Personal communication to the authors.
17. Etcheverry, J. C., in Saye, L.: Doctrina y práctica de la profilaxis de la tuberculosis, Buenos Aires, Editorial Sudamericana, S. A., 1940.
18. Gines, A. R., and Rebull Richieri, V.: Posición de la vacuna BCG en la profilaxis de la tuberculosis, Rev. de tuberc. d. Uruguay **13**: 255-266, 1945.

was at best a "poor take," and more likely "no take." Unfortunately, the mother was not entirely cooperative, so that a Mantoux test could not be performed. The child was eventually taken south, where intractable diarrhea developed. Death occurred soon after his return, at 22 months of age.

A comparison of the incidence of tuberculosis in siblings is given in table 4. Approximately 41 per cent of our entire series in group I were siblings. This constitutes a more exact population for comparison. There were 4 cases of tuberculosis in the vaccinated and no deaths, against 22 cases in the controls with 3 deaths. The morbidity rate per thousand person-years was 5.29 times higher in the nonvaccinated group.

In comparing the time of occurrence of tuberculosis and the type and course of the disease in the vaccinated and in the controls, a distinct contrast is noted (chart 1). There were no cases of tuberculosis in the vaccinated infants 1½ years of age and under, as compared to 9 cases in the controls, 3 of whom died. There were 20 cases of tuberculosis and 6 deaths up to 3 years of age and under in the control group and but 4 cases in the vaccinated. The 1 death has already been discussed.

TABLE 4.—*Incidence of Tuberculosis in Siblings, Noncontact*

	Vaccinated	Nonvaccinated
Total number of children	559	600
Person-years observed	2,712	2,828
Cases of tuberculosis		
Total number	4	22
Rate *	1.47	7.78
Patients hospitalized		
Number	0	9
Rate *	0	3.18
Deaths from tuberculosis		
Number	0	3
Rate *	0	1.06

* Rate per thousand person-years observed.

The duration of the process in the vaccinated group was under one year for all cases, whereas for the controls there were 11 cases out of 25 that presented lesions for longer than twelve months, some lasting over two years (chart 2). Calcification occurred in about 50 per cent of the active lesions of both groups. Six of the 10 controls presented evidence of calcification within two to three years, and 4 not until three to five years. On the contrary, in all 4 cases of the vaccinated group, calcification was noted within two to three years. In addition 3 of the 11 cases in the vaccinated group presented calcification as the first and only roentgen finding as compared to 3 of 39 cases in the controls.

Considering the 7 persons in the control series that died of extensive disease, there were an additional 2 patients in whom the lesions in the lung involved the entire lobe. There were no such cases in the vaccinated group (except the 1 death already described).

From these observations it may be deduced that in the vaccinated group not only is there a suppression of virulent infection, but when infection with virulent organisms does occur, the lesions are less extensive, of shorter duration and calcify earlier than the lesions in the nonvaccinated group.

EFFICACY OF THE VACCINATION, GROUP II

All the children in group II were isolated in foster homes for varying periods of time, depending on the source and the degree of tuberculosis. The control and vaccinated subjects were chosen from a master chart by a person who had only paper knowledge of the cases of infection. In this way no selection between control and vaccinated could be practiced. The discrepancy in the number of cases in the vaccinated and the control group was due to the fact that during the early trial period varying lengths of time of isolation were experimented with and controls were not included. Subsequent to the establishing of a definite schedule, the cases were alternated. To attest that this is an unbiased

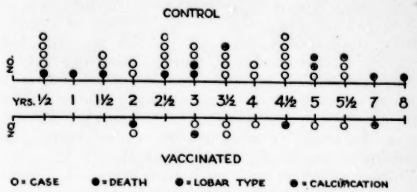

Chart 1.—Incidence of tuberculosis by age groups.

method, a previous study showed that the mother was a source in 58.6 per cent of the vaccinated and 60.3 per cent of the controls; the father in 23.3 per cent and 34.9 per cent respectively. Of the contacts 43.1 per cent had positive sputum in the vaccinated against 39.7 per cent in the controls.

There were 2 cases of tuberculosis in the vaccinated group, in which only 1 patient needed hospitalization, as compared with 5 cases in the control group, in which all patients were hospitalized and 4 died of tuberculosis (table 3). Again recovery in the vaccinated group was within six to twelve months, whereas in the control group the 1 patient that lived had a stormy course for two to three years.

Considering the contact and noncontact group as a whole, there were 13 cases of tuberculosis and 1 death in the vaccinated group as compared with 44 cases of tuberculosis in the controls with 11 deaths.

GROUP III

The student nurses who were vaccinated were allowed to work in the Tuberculosis Hospital, whereas the control negative reactors were not Notwithstanding the

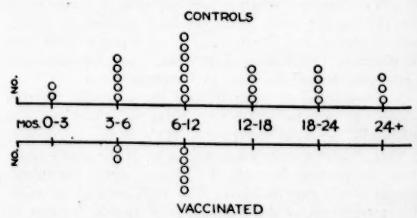

Chart 2.—Duration of active lesions exclusive of deaths and calcification only. Each circle represents a case. (Insufficient roentgenograms were done in 4 cases; lesions were still present in 3 controls.)

discrepancy in the degree of exposure, in none of the 142 vaccinated nurses, over a period of seven years, did pulmonary tuberculosis develop. In contrast there were 3 cases of pulmonary tuberculosis in the 199 controls. All required bed rest and 2 required sanatorium care. There were 3 additional cases of pulmonary tuberculosis among the tuberculin-positive reactors. Tubercle bacilli were said to have been recovered from a cervical

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lymph node of 1 of the vaccinated nurses. She gave a history of drinking raw milk. The lesion did not necessitate hospitalization.

GROUP IV

Medical students at the University of Illinois were first vaccinated in 1939. In the 109 students vaccinated over a four year period, there were no cases of pulmonary tuberculosis. Four cases were reported in the nonvaccinated groups. The complete data are not yet available because of the interruption of the war. Questionnaires are being sent out to obtain more recent information.

GROUP V

In the federal housing project there were 699 children vaccinated and 625 controls who did not react to tuberculin. There were 275 children who reacted to tuberculin at the onset who were not vaccinated. Tuberculin testing and roentgenograms of the chest were done every year. There were no cases of pulmonary tuberculosis in the vaccinated group, whereas among the control negative reactors there were 4 cases of roentgen evidence of the disease, which was considered active in 3. In the tuberculin-positive group there were 2 persons with active tuberculosis of whom 1 died of the disease. Another death from tuberculosis occurred in a child whose tuberculin reaction was not recorded but whose original roentgenogram of the chest was negative. Considering the negative and positive reactors not vaccinated, there were 7 cases of tuberculosis of which 2 were fatal, against no cases of tuberculosis in the vaccinated group.

GROUP VI

Some 4,500 patients at a mental institution were examined roentgenologically and tuberculin tested. Of these 251 did not react to 1 mg. of old tuberculin. The persons with active disease were segregated and the negative reactors were retested seven months later; 84.4 per cent of the 251 had converted. Of the remaining negative reactors, 20 were vaccinated and 15 were kept as controls. In order to identify the vaccinated and the control subjects, they were tattooed with india ink, sterile ink being used and the same type of needle as was used for vaccination. The local reactions to the vaccination did not differ from those described for young adults, although some patients were up to 66 years of age and their habits were unclean. No dressings were used after vaccination. The present status of these patients was submitted by Dr. E. Teller, who was originally associated with this work. There was no pulmonary tuberculosis in the 20 patients vaccinated and 1 case of bilateral minimal arrested pulmonary tuberculosis in 15 controls. The status of the patients was obtained approximately four years following vaccination.

COMMENT

This study represents the longest continuous experiment on BCG vaccination in the United States. From experiences over a period of thirteen years, it can be stated unconditionally that BCG is safe, a fact that has ample verification the world over.[19]

The efficacy of the vaccine has been well documented in this study. In newborn infants of the noncontact group, the tuberculosis rate per thousand person-years was 6.46 for the controls as compared with 1.95 for the vaccinated, or 3.31 times greater for the controls. Considering the 1,159 siblings followed for about 2,800 person-years in the vaccinated and control groups, the rate was 5.29 times greater in the nonvaccinated (table 4). The death rate for the noncontact group was 0.17 for the vaccinated and 1.16 for the controls, or 6.8 times greater in the nonvaccinated. In the contact group the proportions were even more in favor of the vaccinated; the tuberculosis rate was 4.56 times higher in the controls and the death rate was 17.60 for the controls against zero in the vaccinated. Because the populations in the groups being compared are similar, this being especially true for the sibling group, the differences in the groups are highly significant from a statistical standpoint.

In an extensive study in Indians, ages of subjects being 1 to 20 years, over a six year period in which no isolation was effected before or after vaccination, the rate per thousand person-years was 4.7 as compared to 24.3 for the controls (Aronson and Palmer[19a]). Ferguson[19b] of Canada found that in nurses the ratio of vaccinated negative reactors as compared with nonvaccinated negative reactors was 1 to 4.27. His "controls," however, were from a five year period immediately preceding the initiation of vaccination. No isolation was practiced after vaccination. These studies are cited to demonstrate the results obtained in this country following parenteral administration of the vaccine. They cannot be compared with the work being reported in that the age groups and races are different.

Not only were the morbidity and mortality from tuberculosis appreciably reduced after vaccination, but the extent, severity, duration and sequelae of the pulmonary lesions when they did occur in the vaccinated differed from those of the nonvaccinated. In the former, such lesions were less extensive, of shorter duration and calcified earlier.

The vaccination strives to initiate and maintain a positive tuberculin reaction in the recipient. The question of whether this is desirable has been discussed. The protective action of a naturally produced primary complex that is well healed was well brought out by a survey made by one of us[19c] and more recently by Marc Daniels for the Prophit Tuberculosis Survey of Great Britain.[19d] In some twenty reports the world over, the incidence of tuberculosis developing in student nurses (one report included other students) was found by him to be 2.1 per cent (173 cases of 8,202) in those initially positive in reaction to tuberculin as compared to 5.8 per cent (278 out of 4,832) in those originally negative in reaction to tuberculin. In his own study of Great Britain there were 2,120 nursing students originally positive in reaction to tuberculin in 43 of whom, or 2 per cent, tuberculosis developed, against 27 out of 452 negative reactors, or 6 per cent, in whom the disease developed. In children a positive tuberculin reaction following infection with virulent tubercle bacilli may signify a progressive incipient lesion not indicated early by roentgenograms, as well as a current tuberculous environment with opportunities for repeated exposure. In young adults a positive reaction is more likely to indicate a healed primary lesion. It can readily be understood why a positive tuberculin reaction in children, if caused by natural infection, offers a poor

19. (*a*) Aronson, J. D., and Palmer, C. E.: Experience with BCG Vaccine in the Control of Tuberculosis Among North American Indians, Pub. Health Rep. **61:** 802-820, 1946. (*b*) Ferguson, R. G.: BCG Vaccination in Hospitals and Sanatoria of Saskatchewan, Canad. J. Pub. Health **37:** 435-451, 1946. (*c*) Rosenthal, S. R.: Use of BCG Vaccination Among Medical and Nursing Students, Hospitals **17:** 75-78, 1943. (*d*) Daniels, M.: Primary Tuberculous Infection in Nurses: Manifestations and Prognosis, Lancet **2:** 165-170, 201-204 and 244-246, 1944. Footnotes 1 and 2.

prognosis. It would thus seem logical to substitute BCG, which is avirulent and in which the dose can be controlled, for virulent uncontrollable natural infection.

Another timely question is: What portion of our population should receive BCG vaccination? This and other studies indicate that for the time being, at any rate, those who benefit most by the vaccination are susceptible races (such as Negro and Indian) and those unduly exposed to tuberculosis of all races, in all age groups. It is again stressed that those who are vaccinated should have a period of at least one month before and after vaccination when there is no direct contact with virulent tubercle bacilli.

It has been stated that the decline in the death rate from tuberculosis in the United States has been so precipitous (from 194.4 to 40.1 per hundred thousand in 1900 and 1945 respectively)[20] that no further measures are needed to reduce the incidence of the disease other than those that are already in practice. In 1926 the rate for 1940 was predicted to be 20 per hundred thousand[21]; in 1941 it was predicted that substantial elimination of the disease was in sight by 1960.[22] These predictions have fallen pitifully short of their goal. Granted that the death rate from tuberculosis for all ages is seventh on the list of deaths from all causes, between the highly productive ages of 18 to 40 years it ranks first. Some supplement, therefore, is definitely needed to augment our present methods of tuberculosis control.

The need for BCG vaccination will probably become more and more important as the incidence of tuberculosis drops, for we may again approach a relatively virgin soil in human beings for the tubercle bacillus. What may happen in a susceptible people is illustrated in a small tuberculosis epidemic that occurred in a secondary girls' school in Denmark in pupils aged 12 to 19 years.[10] In January and February of 1943 an influenza-like epidemic broke out, and because there was associated erythema nodosa, tuberculosis was suspected. Fortunately, a tuberculosis control program had been in effect for some years, and the status of each pupil was known as regards the tuberculin reaction and roentgenogram of the chest. Before the outbreak it was known that of the 368 students, 130 were tuberculin positive in reaction, and 105 tuberculin negative, and 133 had been vaccinated with BCG. Of the 105 tuberculin-negative reactors, 70 converted during a period of a few months; of the 70, 41 showed roentgen changes, and of the latter tubercle bacilli were demonstrated in 37. There were 7 cases of definite pulmonary disease, or 6.7 per cent. Of the 133 vaccinated with BCG, there was pulmonary disease in only 2, or 1.5 per cent, whereas in the naturally positive reactors there were 4 cases, or 3.5 per cent. The source case was found to be a female teacher in whom minimal processes were demonstrated in one apex together with a positive gastric lavage. She taught class in a badly ventilated basement room. It is of interest that the rate of conversion was high not only in those pupils whom this teacher taught, but also in those pupils who occupied the same room but were not in contact with the teacher in question. The cases of genuine pulmonary tuberculosis, of which there were 13, practically all occurred in the teacher's own class (12 out of 13). Better than 50 per cent of all the pupils in the initially tuberculin-negative, BCG-vaccinated and initially tuberculin-positive groups were exposed to the infected teacher. The percentage of conversion in the originally tuberculin-negative reactors was 86.8 per cent for those in contact with the teacher and 58.5 per cent for those in her classroom only.

In vaccinated adults and children in the Tice Laboratory study, no pulmonary tuberculosis occurred after three to seven years, whereas the expected morbidity rate was noted in the controls. This is a preliminary report for these groups.

The persistence of the tuberculin reactivity following a single vaccination in newborn infants was almost universal up to three and one-half and four years and practically 80 per cent after six and one-half years. In young adults it was 88.6 per cent after three years. It cannot be definitely stated that the results obtained in this study as far as the reaction to tuberculin was concerned were due entirely to the vaccination, as a high degree of conversion occurred in the controls soon after they entered this study.

The application of the vaccine by the multiple puncture scarification method has minimized the complications to a negligible level. This, plus the fact that the vaccine and the scarifying needle are put up in capillary tubes much the same as for vaccinia, makes this form of vaccination admirably suited for general use.

The United States Public Health Service has selected the Tice Laboratory as the central one for the production of BCG for its use. In this capacity the Tice Laboratory has supplied vaccine for the government BCG vaccination programs in Georgia and in Michigan.

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SUMMARY

The application of BCG vaccination to all age groups is a safe and effective procedure.

In 2,831 newborn infants living in the poorest districts of Chicago but not in household contact with tuberculosis, there were 11 cases of tuberculosis in the vaccinated against 39 in the controls. The rate per thousand person-years was 3.31 times as great in the controls as in the vaccinated. There was 1 death from tuberculosis in the vaccinated against 7 in the controls, or a difference in the rates of 6.8 times.

In 1,159 siblings the tuberculosis rate per thousand person-years was 5.29 times as great in the controls as in the vaccinated.

Among 256 newborn infants, when tuberculosis was present in the household and when isolation in foster homes was practiced in the controls and vaccinated alike, there were 2 cases of tuberculosis in the vaccinated as compared to 5 in the controls. The rate was 4.56 times as great in the controls. There were 4 deaths in the controls and none in the vaccinated.

Considering the noncontact and contact groups as a whole, there were 13 cases of tuberculosis with 1 death in the vaccinated group as compared to 44 cases of tuberculosis with 11 deaths in the controls.

In a preliminary report on children in a federal housing project, in nursing and medical students and in patients of all ages in a mental institution, there were no cases of pulmonary tuberculosis in the vaccinated group followed for three to seven years. The expected tuberculosis rate was present in the control groups.

20. Linder, F. E., and Grove, R. D.: Sixteenth Census of the United States: Vital Statistics in the United States 1900-1940, United States Department of Commerce, Bureau of the Census, 1943. Patterson, R. G.: The Evolution of Official Tuberculosis Control in the United States, Pub. Health Rep. **62:** 336-341, 1947.

21. Krause, A. K.: Tuberculosis the Fifth Cause of Death in United States, Tubercle **7:** 442-448, 1926.

22. Dublin, L. I.: 1941 Closes with Distinctly Good Health Record, Diplomate **14:** 35-37, 1942.

By the use of the multiple puncture method, practically all complications were avoided; tuberculin reaction conversion was rapid (within one month) and universal.

A positive tuberculin reaction following a single vaccination was present in 92.6 per cent after three and one-half to four years and 79.85 per cent after six to six and one-half years in children vaccinated at birth and 88.6 per cent in student nurses at the end of their training, three years after vaccination.

ROLE OF TRANSFUSION IN THE ETIOLOGY OF ERYTHROBLASTOSIS

A Warning to Physicians

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Since the role of the Rh factor and isoimmunization in the production of erythroblastosis was first pointed out by Levine [1] and Wiener [2] more than seven years ago, this phenomenon has been of great concern to the physician and layman alike. It is amazing that such widespread interest should be centered on a disease which is extremely rare, since clinically recognizable erythroblastosis fetalis probably does not occur in the usual obstetric clinic in more than 1 in 300 deliveries; and, inasmuch as the infant mortality from this disease is in the neighborhood of 50 per cent, it can be estimated that the chances of an infant dying from this condition are less than 1 in 600 deliveries. The theory enunciated by Levine is simple and straightforward. If an Rh-positive man is married to an Rh-negative woman, which combination makes up about 12 per cent of the marriages, the infant will in the majority of instances be Rh-positive. The woman, being Rh-negative, is capable of being sensitized or producing antibodies to the Rh-positive cells of her unborn child and, thus, when these antibodies cross the placenta they hemolize the blood of the infant, producing the varied manifestations of erythroblastosis. The immunology of isoimmunization and the genetics of the Rh factor have provided a fertile field for many investigators whose names are well known. A point which has been mentioned only casually by Levine [3] and Diamond,[4] but has not received the emphasis it deserves, is the role of transfusion in the production of this syndrome. This is all the more pertinent because of the recent development of blood banks and the more and more frequent use of transfusions. The great increase in the number of transfusions given at the Johns Hopkins Hospital is illustrated by the fact that 1,100 transfusions were given in 1939 as compared with 5,585 in 1946, a fivefold increase.

There are but two ways by which an Rh-negative woman can be sensitized to Rh-positive cells and thus give birth to an erythroblastotic child. The first of these is by repeated bearing of Rh-positive children. This process gives her a gradually ascending titer of Rh antibodies, producing after several pregnancies mild and then more and more severe erythroblastosis. In such an event her first and often her second child are spared. The second means by which such a woman may become sensitized is by the administration of an Rh-positive transfusion. This will produce no outward reaction if she has not been previously immunized but serves as a much more powerful immunizing agent than the repeated bearing of Rh-positive children. Even a small transfusion will give a high and persistent antibody titer. Women so sensitized produce Rh-positive children with the severest form of erythroblastosis who usually do not survive. If they are in the 38 per cent who have homozygous Rh-positive husbands, they will be fortunate indeed to have 1 living child. Since 1937 there have been 27 cases of erythroblastosis in the Department of Obstetrics of the Johns Hopkins Hospital. These are shown graphically in table 1. The incidence in that year was 1 in 1,732 deliveries, while in 1946 the incidence was 1 in 348 deliveries. It is doubtful that the diagnosis was missed during that period, and while the apparent increase in incidence may be due somewhat to selection of cases for admission, it must also be admitted that there may be a real increment in the incidence of the disease. Since the percentage of Rh negativeness in the population is fixed, such an increment must be due to an increase in the incidence of sensitization of the mothers, and such a phenomenon may well be related to the increased incidence of transfusion known to have taken place. Of the 27 cases of erythroblastosis, the 7 following gave a history of transfusion:

TABLE 1.—*Incidence of Erythroblastosis, Johns Hopkins Hospital, 1937-1946*

Year	Deliveries	Cases	One/Deliveries
1937	1,732	1	1,732
1938	1,935	0	.....
1939	1,876	4	469
1940	1,831	2	915
1941	1,704	2	852
1942	1,903	2	951
1943	1,880	2	940
1944	1,843	3	614
1945	2,020	4	505
1946	2,436	7	348
Total	19,160	27	710

HISTORIES OF CASES

CASE 1.—The patient was a 40 year old para 3-3-0-0-1.[5] Her first child was delivered in 1927 by cesarean section because of premature separation of the placenta. The child was never in good condition and died at 18 months of life. After the operation the patient received one transfusion. Her second child was delivered in 1937 by low forceps. It weighed 2,370 Gm. and was jaundiced and anemic at birth. It received a few transfusions while in the hospital and was discharged weighing over 3,000 Gm. Soon after going home it was found dead in its crib; it presumably died of some cerebral damage due to erythroblastosis. Her last child was delivered in 1939 by low forceps and weighed 2,890 Gm. At birth it had 1,890,000 red cells per cubic millimeter and was jaundiced. It received multiple transfusions and survived and is living and well today.

CASE 2.—The patient was a 34 year old para 2-2-0-0-1 whose first pregnancy in 1942 terminated in a stillborn infant, the

From the Department of Obstetrics, Johns Hopkins University School of Medicine and the Johns Hopkins Hospital.

1. Levine, P., and Stetson, R. E.: Unusual Case of Intra-Group Agglutination, J. A. M. A. **113**: 126 (July 8) 1939.
2. Wiener, A. S., and Peters, H. R.: Ann. Int. Med. **13**: 2306, 1940. Landsteiner, K., and Wiener, H. S.: Proc. Soc. Exper. Biol. & Med. **43**: 22, 1940.
3. Levine, P., and Waller, R. K.: Blood **1**: 143, 1946.
4. Diamond, L. K.: New England J. Med. **232**: 475, 1945.
5. The numbers following para indicate in order total pregnancies, full term infants, premature infants, abortions and living children.

fetus having died in utero on the day before the onset of labor. She had a postpartum hemorrhage because of an adherent placenta and was given one blood transfusion. She was Rh-negative and her husband homozygous Rh-positive. Her second pregnancy in 1944 terminated in a living infant which had pronounced erythroblastosis with anemia and jaundice. This infant was successfully treated by repeated transfusions and is now living but is spastic. She was seen for this pregnancy at about the tenth week, at which time she showed blocking antibodies (4 plus) with glutinins of 96 units in plasma. Because of the uncertainty of another erythroblastotic child the pregnancy was interrupted.

CASE 3.—The patient was a white primigravida aged 20 whose delivery was due by dates in December 1945. She was Rh-negative and her husband was homozygous Rh-positive. She received two transfusions for severe epistaxis in 1943. She was delivered by low forceps on November 10 of an edematous and jaundiced infant. The child did not survive more than two hours in spite of multiple transfusions.

CASE 4.—The patient was a 32 year old para 2-2-0-0-1. She was Rh-negative and her husband was homozygous Rh-positive. Eight years prior to the present pregnancy she was deliverd of a normal Rh-positive child. One year later she had a partial gastrectomy for a duodenal ulcer and at that time she had three transfusions. To each of these she had a severe reaction. Near term in the present pregnancy she had glutinin titer of 64 units and blocking antibodies (4 plus). She was delivered by low forceps of a 3,200 Gm. child in poor condition. The child had severe jaundice and low hemoglobin level and in spite of repeated transfusions did not survive. The diagnosis of erythroblastosis was confirmed at autopsy.

CASE 5.—The patient was a 38 year old para 3-3-0-0-3 who through a laboratory error was thought to be Rh-positive. Her first child, born in 1939, and a second, born in 1942, were both Rh-positive and were living and well. Following her second delivery she had a postpartum hemorrhage for which she received one transfusion. She was delivered at term by low forceps of a 3,120 Gm. child in November 1946. The child was in poor condition and showed decided pallor and some jaundice at birth. The diagnosis of erythroblastosis was made and confirmed by examination of the infant's blood. On reexamination of the patient she was found to be Rh-negative and her husband was homozygous Rh-positive. She had a glutinin titer of 64 units. The child was severely ill and after receiving multiple transfusions and a long hospital stay left the hospital in good condition. The jaundice was never severe and serious anemia never developed. It was discharged from the hospital without requiring any transfusion.

CASE 6.—The patient was a 30 year old para 2-2-0-0-1 who was delivered in 1934 of a normal Rh-positive infant. She was Rh-negative and her husband homozygous Rh-positive. In 1941, after a pelvic operation, she was given one transfusion. During her present prenatal period blocking antibodies (3 plus) and a glutinin titer of 512 units in plasma developed. She was delivered at term in September 1945 of a living 3,230 Gm. infant which had congenital hydrops, jaundice and anemia. There were gross placental changes. The child did not survive more than two hours and the diagnosis of erythroblastosis was confirmed at autopsy.

CASE 7.—The patient was a 22 year old primigravida who at the age of 2 months received one transfusion of 170 cc. of blood for dysentery. She was Rh-negative and her husband was heterozygous Rh-positive. Her due date in the present pregnancy is March 1946. On February 22 she showed a glutinin titer of 24 units in plasma. She also had blocking antibodies (4 plus). She was delivered on February 28 of a 3,120 Gm. male infant in good condition. The baby became jaundiced at 5 hours and showed both agglutinins and glutinins in its plasma.

TABLE 2.—*Effect of Transfusion on the Childbearing Career of Nine Patients, 1937–1947*

Patient	Before Transfusion: Living Infants	Before Transfusion: Dead Infants	Reason for Transfusion	Antibodies: Agglutinin	Antibodies: Blocking	Antibodies: Glutinin *	After Transfusion: Erythroblastotic Infants: Normal Infants	After Transfusion: Erythroblastotic Infants: Lived	After Transfusion: Erythroblastotic Infants: Died	Future Pregnancies †
1	0	1	P. S.‡	Not determined	Not determined	Not determined	0	1	1	0
2	0	1	P. P. H.§	0	++++	96	0	1 Spastic	0	0
3	0	0	Epistaxis	Not determined	Not determined	Not determined	0	0	1	0
4	1	0	Gastrectomy	0	++++	64	0	0	1	0
5	2	0	P. P. H.	0	++++	48	0	1	0	0
6	1	0	U. S.¶	0	+++	512	0	0	1	0
7	0	0	Dysentery	0	++++	24	0	1	0	50.0
8	0	0	Arthritis	0	++++	96	1	0	0	50.0
9	1	0	P. P. H.	0	++	3	1	0	0	50.0
Total	5	2	.....	..	.....	..	2	4	4	....

* Cells suspended in plasma.
† Prognosis for future normal children as determined by genotype of husband (homozygous 0 per cent; heterozygous 50 per cent).
‡ Premature separation of placenta.
§ Postpartum hemorrhage.
¶ Suspension of uterus.

The summary of these cases can be seen in table 2. The following 2 cases represent Rh-negative women with heterozygous Rh-positive husbands and a carry-over of agglutinins from the transfusion. They are added to table 2 although they gave birth to normal Rh-negative infants.

CASE 8.—The patient was a 27 year old primigravida who was given two blood transfusions for anemia and arthritis in 1942. She was Rh-negative and her husband was heterozygous Rh-positive. In addition to the transfusions in 1942 she was given another transfusion in 1945, at which time she had a severe reaction with hematuria. During this pregnancy a glutinin titer of 192 units developed, and she had blocking antibodies (4 plus). She was delivered at term in November 1946 of a 3,480 Gm. infant which was Rh-negative and which showed no erythroblastosis.

CASE 9.—The patient was a 26 year old para 2-2-0-0-2 who was Rh-negative and whose husband was heterozygous Rh-positive. She was delivered in 1944 of a normal infant which is living and well. The delivery was followed by a postpartum

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hemorrhage for which she received one transfusion. During this pregnancy she showed blocking antibodies (4 plus), but more than 12 units of glutinin never developed. She was delivered at term in January 1947 of a 3,090 Gm. Rh-negative infant in good condition.

Nine Rh-negative women are presented who had received previous blood transfusions and who subsequently delivered children with erythroblastosis or in whom antibodies developed which endangered their future childbearing careers. These 9 women had had 5 normal children prior to their transfusions but had only 2 normal infants thereafter. Both the normal children born after transfusion were Rh-negative, these women having heterozygous husbands. The patients with homozygous mates had no normal children after transfusion, and of the 8 erythroblastotic infants born to them the expected survival of 50 per cent occurred. Hence the subsequent childbearing of all these patients had been seriously jeopardized, especially those with homozygous husbands. At least 1 of these latter has requested and received sterilization for this reason.

It might well be argued that all but 3 of these patients had one or more pregnancies prior to the transfusion

TABLE 3.—*Interval Between Transfusions and Birth of Erythroblastotic Child in Seven Patients*

Patient	Age at Transfusion	Year of Transfusion	Number of Transfusions	Interval to Birth of Erythroblastotic Infants, Years
3.....	17	1943	2	2
2.....	30	1942	1	2
5.....	34	1942	1	4
6.....	25	1941	1	5
4.....	25	1939	3	7
1.....	21	1927	1	10
7.....	2 months	1925	1	21

and that the pregnancy alone might well be sufficient to immunize them. Certainly this fact cannot be denied, but it is interesting to note that a history of previous transfusion occurs in but 2 per cent of our patients, while in the 27 instances of erythroblastosis a history of transfusion was present in 7 women or 26 per cent; and all in all the evidence is strong that transfusion does play an important role in the production of erythroblastosis. With the increased use of transfusion the chance of unwittingly administering Rh-positive blood to Rh-negative women is definitely increased. Since such transfusions may be disastrous to future childbearing, even though many years may intervene, they can only be regarded as reprehensible; and in our opinion a high degree of negligence may be charged if transfusion is ever given to a female child, or women in the childbearing age, without first determining the Rh compatibility. In cases of dire emergency when time does not permit Rh determinations, only Rh-negative blood should be given.

CONCLUSION

The obstetric experiences of 9 Rh-negative women are reviewed who gave histories of previous blood transfusions. As the result of these transfusions the subsequent childbearing careers of these patients were gravely jeopardized. There is need to reemphasize the fact that Rh compatibility should be determined for all females prior to transfusion and only Rh-negative blood should be used in negative cases.

KALA-AZAR

Report of a Case Showing Unusual Leukocyte Response and Prolonged Incubation Period

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Prior to the onset of World War II, kala-azar (visceral leishmaniasis) was a disease discussed only by those few who specialized in tropical medicine and by members of teaching institutions when presenting cases of splenomegaly for differential diagnosis. In the latter instance, kala-azar was usually discarded as a possible diagnosis because the patient had never been out of the United States. Today this may not be true. During the recent war and continuing even to the present time several hundred thousand American troops were and are stationed in the several parts of the world where kala-azar is endemic, the most important of which are Eastern India, Burma, Northeastern China, Southern Italy and the Mediterranean coast of North Africa. Because of this and because the incubation period of the disease may be prolonged, the possibility of the occurrence of clinical kala-azar among former servicemen is more than theoretic.

Kala-azar is caused by the protozoan organism Leishmania donovani. It is agreed by most workers that the organism is transmitted to man by the bite of one of several species of the sandfly. On culture the organism develops in a flagellate form, while in man the organism appears as the Leishman-Donovan body. Strong [1] described this form as "round or oval bodies 2-5 microns in diameter. The nucleus is relatively large and peripherally placed; the kinetoplast is smaller, rod-shaped, or oval, and set at a tangent to the nucleus. A short, slender filament, the axoneme, is sometimes seen extending from the blepharoplast to the periphery. In a Romanowsky stain, the cytoplasm is faintly blue, the nucleus appears as a mass of bright red granules, and the kinetoplast is deep reddish purple."

Clinically there is no typical picture. The fever may be alternating, remittent or intermittent. In some cases, however, there is a double or triple daily rise in the temperature, which is said to strongly suggest the diagnosis of kala-azar. It has also been observed in this disease that a patient may have a temperature of as much as 102 F. and state that he feels well. The onset of the disease may be sudden with high temperature, chills and vomiting, or it may begin gradually with a low grade fever and relatively mild general symptoms. The onset may be easily confused with typhoid or malaria, more particularly the latter, as malaria is endemic in many of the areas where one may become infected with kala-azar. The incubation period varies from ten days to eighteen months. The disease produces progressive loss of weight with noticeable wasting of the muscles. Enlargement of the spleen does not usually occur until after the first month of the disease.

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NOTE: The Department of Pathology, Baylor University School of Medicine, assisted in obtaining the photomicrograph of the bone marrow specimen in this case.

1. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 7, Philadelphia, The Blakiston Company, 1944, vol. 1, pp. 229-319.

The hemogram is said to offer some aid in the diagnosis of kala-azar. There is anemia present, usually becoming evident after the first month of the disease. The most dramatic changes occur in the white cell count. The total number of white blood cells is greatly reduced—in the majority of cases to less than 3,000 per cubic millimeter. The differential picture reveals a reduction in the polymorphonuclear leukocytes and an increase in the number of the large mononuclear cells and lymphocytes. However, in the case to be reported there was a decided shift to the left in the differential count. Another important finding is the alteration in the ratio of the white blood cells to the red blood cells. The normal ratio of 1:666 or 1:750 is only rarely observed. In cases of kala-azar the ratio of these cells is usually in the range of 1:1,000 or 1:1,500.

Blood chemical studies reveal an elevation of the globulin fraction of the blood serum. The euglobulin fraction is often considerably elevated and may account for 40 to 50 per cent of the total globulin. The formaldehyde gel test is positive in result in cases of well established kala-azar and gradually reverts to normal as recovery ensues. A similar reaction with a pentavalent antimony compound such as ethylstibamine ("neostibosan") may give additional presumptive evidence for the diagnosis of kala-azar.

There is only one means for the positive diagnosis of this disease and that is to demonstrate the causative organism in tissue taken from the patient. In the vast majority of patients this is simply and easily done if the possibility of such a diagnosis is kept in mind and searched for. The most simple and least dangerous procedure is needle aspiration of the sternal bone marrow. This technic is practically devoid of danger and if properly done will demonstrate the parasites in a high percentage of cases. An alternative to this procedure is the surgical biopsy of the sternum, the specimen of marrow being obtained after the sternum has been trephined. Splenic puncture is generally conceded to give the highest number of positive smears, but this technic presents definite hazard to the patient, and, in cases in which the spleen is not palpably enlarged, it is almost impossible to perform. Meleney [2] stated that aspiration of the liver demonstrates the organisms in a high percentage of cases and claimed that the procedure is not unduly dangerous if carefully and properly performed. Demonstration of the parasites in the peripheral blood is reported but is infrequent. Culture of the organisms on Nicolle, Novy and McNeal mediums may be done, material obtained by any of the procedures mentioned being used. Also a specimen of blood may be obtained under sterile technic in oxalate, and after the cells have been spun down, the buffy layer of leukocytes may be inoculated on the mediums. In culture the parasite develops in the flagellate form. It has been suggested that culture be attempted in any case in which the diagnosis is suspected.[3]

Several pentavalent antimony compounds are available for the treatment of kala-azar. Many workers prefer ethylstibamine, as it is reported to be less toxic than other drugs and its therapeutic efficiency is high. This drug may be given intravenously or intramuscularly, the intravenous route being preferred. The first dose should be 0.1 or 0.2 Gm., being increased to 0.3 Gm. as a maintenance dose. The injections may be given daily or less often, depending on the reaction of the patient. Total dosage recommended varies from 3.5 Gm. to 5 Gm. The larger figure may be exceeded in cases in which the disease is more resistant to treatment. The drug is relatively safe, but certain reactions may be observed, the most common of which are nausea and vomiting that occur shortly after the injection. If the patient remains at complete bed rest and does not eat for one to two hours after the injection, these symptoms will often be minimized. If vomiting persists, smaller doses of the drug should be given. Symptoms resembling anaphylactic shock have been reported, usually after several injections have been given. Urticarial rash, laryngeal edema, cyanosis and signs of asthma may develop. Epinephrine will relieve these symptoms, but since these symptoms, which may result after the use of any of the antimony compounds, will often recur when that particular drug is again administered, it has been suggested that a different antimony compound be used to complete the treatment.

Variations in Peripheral Blood Picture

Date, 1946	Red Cells	White Cells	Hemoglobin, %	Basophils	Eosinophils	Myelocytes	Juvenile	Stabs	Segmenters	Lymphocytes	Monocytes
September 23	.....	1,800	78	..	3	3	28	22	13	29	2
September 24	4,470,000	2,400	81	1	..	..	44	14	5	30	4
September 30	4,650,000	5,000	82	3	..	..	17	23	18	36	3
October 1	4,600,000	2,150	79	2	1	5	14	23	14	37	4
October 3	4,450,000	5,000	85	1	..	..	1	29	44	20	5
October 11	4,500,000	4,300	88	3	2	..	1	9	41	35	9
October 18	5,110,000	8,100	85	2	20	..	2	2	34	38	2
October 25	5,430,000	5,500	89	2	19	..	..	1	29	38	11
November 1	5,020,000	5,850	88	..	2	..	..	..	53	41	4
December 6	4,970,000	5,150	97	2	4	..	..	2	33	55	4
September 26	Platelets 111,800										
September 25	Bone marrow: Premyelocytes 1.5%; myelocytes 8.0%; juveniles 31.5%; bands 12.0%; segmenters 9.0%; lymphocytes 11.5%; normoblasts 23.5%; megaloblasts 1.5%; eosinophils 1.5 %										

REPORT OF A CASE

A pilot officer, aged 25, was admitted to the hospital on Sept. 21, 1946. Symptoms began September 7 with mild generalized malaise and mild intermittent pain in the left upper part of the abdomen. His appetite decreased and he noted increasing fatigue. He reported to his station dispensary on September 16 because of the progression of these symptoms. Acetylsalicylic acid, acetophenetidin and caffeine tablets were prescribed. On September 18 a roentgenogram of the chest was reported normal. The morning of September 19 the patient felt somewhat improved, but that afternoon he noted a cold tingling sensation in his hands, and shortly thereafter a chill developed, after which his oral temperature was 104 F. Without laboratory studies the patient was treated with quinacrine, 0.1 Gm. three times daily. At about 2 a. m., September 20, he had a second chill followed by vomiting. The vomitus consisted of the food eaten at the previous evening meal. He had two diarrhea stools and there were repeated chills approximately every six hours

2. Meleney, H. E.: Early Diagnosis of Kala-Azar, J. A. M. A. **129**: 150-151 (Sept. 8) 1945.

3. Packchanian, A.: Leishmaniasis: Cultivation of Leishmania Tropica from Two American Soldiers Who Had Returned to the United States from Near East, J. A. M. A. **129**: 544-547 (Oct. 20) 1945.

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until the morning of September 21, when he again reported to his dispensary. Oral temperature at this time was 101 F., and he was then hospitalized with a presumptive diagnosis of malaria. There had been weight loss of 20 pounds (9.1 Kg.) in the two weeks prior to hospitalization.

Past History.—He had experienced no similar symptoms prior to the onset of the present illness. He served overseas as a fighter pilot in the China-Burma-India theater from December 1943 to April 1945. There was no history of previous attacks of malaria. He experienced one episode of diarrhea lasting one week in May 1944 while stationed in India. No specific etiologic agent was found, and the diarrhea responded to nonspecific treatment.

Examination.—The patient was acutely ill and somewhat emaciated, and showed recent loss of weight. There was a slight injection of the membrane of the throat and a mild gingivitis was present. There was no nuchal rigidity; no evidence of superficial lymphadenopathy, rash or petechial eruption. The heart was normal, and the lungs completely clear. Blood pressure was 110 systolic and 64 diastolic. The abdomen was soft and flat, and neither the liver nor the spleen was palpated. No abdominal masses were evident. There was slight tenderness on deep palpation in the left upper part of the abdomen. The remainder of the physical examination revealed no abnormalities.

Quinacrine was continued, 0.1 Gm. three times a day, in spite of a negative malaria smear, because it was felt that the low initial dosage given this patient may have cleared the parasitemia and yet have been insufficient to cause a remission of clinical symptoms. On September 23 there was a total white blood cell count of 1,800 with 29 per cent lymphocytes, 2 per cent monocytes, 13 per cent segmented polymorphonuclear cells, 25 per cent band forms, 28 per cent juveniles and 3 per cent myelocytes. On this date a second study for malaria failed to reveal the presence of parasites. Because of this and because the blood picture indicated possible leukemia and/or severe infection as yet undiagnosed, quinacrine was discontinued; penicillin, 50,000 units intramuscularly every three hours, and liver extract, 3 cc. daily, were administered. Blood counts continued to show profound leukopenia with a considerable shift to the left in the differential picture. There was only mild anemia noted at any time. The table shows the data on the blood during the entire period. Repeated examinations of the urine, including a test for Bence-Jones protein, revealed no abnormality. An aspiration biopsy of sternal bone marrow was made on September 25, and stained smears revealed a normal differential cell count. No organisms were seen in the five slides examined. A platelet count on September 26 was 111,800 (normal 250,000 to 500,000). The patient's temperature continued on a septic course (fig. 1). Many blood cultures remained sterile after prolonged incubation. An organism having the carbohydrate reaction of Salmonella eastbourne was isolated from the stool on two occasions. Agglutinations for typhoid, paratyphoid, undulant fever and heterophil antibody were negative on September 24 and September 30. On the latter date the Weil-Felix reaction and agglutination with Pasteurella tularensis were also negative. On October 2, roentgenograms on the chest and abdomen were normal—there was no evidence of enlargement of the spleen or liver. On October 3, a biopsy specimen from the upper part of the sternum was obtained by trephine. Several impression smears were made from the marrow, and after staining with a diluted Giemsa stain, examination revealed many intracellular and extracellular organisms which were typical of the Leishman-Donovan bodies of kala-azar (fig. 2). Treatment with ethylstibamine was begun on October 5, the patient receiving 0.2 Gm. intravenously on this date. Daily thereafter, through October 20, he received 0.3 Gm. intravenously. A total of 4.7 Gm. was given; no adverse effects were observed.

Response to treatment was dramatic; the temperature returned to normal after three days, appetite greatly improved—four meals daily were enjoyed—and there was a progressive gain in weight from 130 pounds (59 Kg.) to 152 pounds (68.9 Kg.). The table shows the improvement in the peripheral blood. Penicillin was continued until October 5, as a precaution against secondary infection. Attempts to culture marrow blood and peripheral blood on mediums developed by Nicolle, Novy and McNeal were unsuccessful. On December 3 the patient was returned to duty; no evidence of disease was present. He was, however, instructed as to the symptoms and signs of relapse of the disease and warned of the possible late occurrence of post-kala-azar cutaneous leishmaniasis.

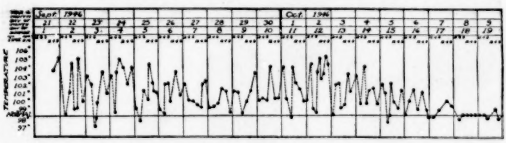

Fig. 1.—Temperature chart showing double and triple daily elevations. The temperature was determined at 12, 4 and 8 a. m. and 12, 4 and 8 p. m. (from left to right in each column). Treatment with ethylstibamine started on October 5.

COMMENT

After the correct diagnosis was made in this case, a more complete history of the specific areas visited during the patient's tour of overseas duty was obtained in an attempt to estimate the incubation period. He was in several areas in which kala-azar is known to be endemic. In May 1944 he was located on the southeast coast of India near the Burma border. From November 1944 until February 1945 he was in the vicinity of Sien, China. This town is located just south of the bend of the Yellow River and is within the area of China where this disease is endemic. While returning to the United States via air transport the patient spent one day each in Abadan, Iran, and Cairo, Egypt. These cities are both located in areas where cutaneous leishmaniasis is endemic and where an occasional case of the visceral disease is reported. It is our belief, because of the longer period of exposure while this officer was stationed in China, that his disease was most likely contracted some time between November 1944 and February 1945. On this supposition, the incubation period in this case was at least nineteen months, if it is assumed that the patient became infected only shortly before he left this area. The patient was in Abadan on April 1, 1945 and in Cairo on April 2, 1945. He arrived in Casablanca in the western part of North Africa on April 3, 1945 and left this area by air on April 10, 1945, arriving in the United States on April 11, 1945. If the time from April 10, 1945, when the patient left the African continent and any possible source of infection, until the onset of symptoms on Sept. 7, 1946 is considered, an incubation period of approximately seventeen months is indicated. The prolonged period of incubation in this case is unusual, and we have been able to find only 1 such case previously reported.[4]

The possibility of prolonged periods of incubation in kala-azar serves to emphasize the importance of this disease in the United States. It must be strongly considered in cases of obscure fever in persons who have spent time in areas where kala-azar is endemic.

The second unusual feature of the case presented in this report is the considerable shift to the left observed in the differential white cell count. It is reported that this disease produces a relative lymphocytosis.[5] This was never observed in the case under discussion, and

4. Napier, cited by Strong.[1]

5. Since preparation of this paper, two reports have appeared in which cases of kala-azar with similar blood pictures have been observed: Waud, S. P., and Kruger, S.: Visceral Leishmaniasis: Report of a Case, New England J. Med. **236**: 63 (Jan. 9) 1947. Ecker, H. D., and Lubitz, J. M.: Kala-Azar in the United States: Review of the Literature and Report of Two Cases; Stilbamidine Treatment, Ann. Int. Med. **26**: 720-733 (May) 1947.

there was no evidence at any time of other infection which might have explained the blood picture observed.

The one typical finding in this case was the temperature course. It is said that two or three spikes in the temperature every twenty-four hours is only rarely observed in diseases other than kala-azar. Figure 1 clearly shows this finding on several days.

SUMMARY

A brief review of kala-azar is presented, showing its symptoms, signs, methods of laboratory diagnosis and treatment. An unusual case of kala-azar with an incubation period of at least seventeen to eighteen months and with unusual hematologic observations is reported. It is believed that this case will help to emphasize the fact that kala-azar is now a disease which must be considered in the differential diagnosis of fevers which may occur in patients living in the United States who give a history of spending time in any of the areas of the world where this disease is endemic.

Fig. 2.—Photograph of bone marrow showing intracellular Leishman-Donovan bodies.

Smallpox Vaccination and Encephalitis.—It is well known that encephalitis occasionally follows vaccination. When it is due to vaccination, it almost invariably occurs eleven to fourteen days later. It may occur up to thirty days later, but this is exceedingly rare. From the beginning of April, when the vaccination program was instituted, until the second week of June, 50 possible cases of encephalitis were reported to the Health Department. Four of these cases were ruled out as definitely not encephalitis. In the remaining 46 cases the diagnosis was considered probable. Eight of these 46 individuals died. A diagnosis of postvaccinal encephalitis can be made with certainty only after microscopic examination of the brain tissue. Brain tissue of the 8 fatal cases was examined, and in none of them were the characteristic lesions of postvaccinal encephalitis found. Autopsy showed that 2 of the deaths were caused by tuberculous meningitis, 1 by a brain tumor, 1 by coronary sclerosis, and 4 probably by cerebral lesions. The Health Department has had no proof of any death due to postvaccinal encephalitis in its vaccination campaign.—Weinstein, Israel, M.D., An Outbreak of Smallpox in New York City, *American Journal of Public Health*, November, 1947.

STREPTOMYCIN IN THE THERAPY OF GRANULOMA INGUINALE

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Streptomycin has been found to be active principally against certain gram-negative organisms and acid-fast bacilli. Its trial in the management of granuloma inguinale, while not entirely justified in view of the controversial concept of the nature of the pathogenic agent, was warranted on the basis that the need for a more effective and specific form of therapy of granuloma inguinale was greatly desired. Before the advent of the antibiotics the modern therapy of granuloma inguinale generally involved the use of one of a number of antimony compounds. These have varied from the intravenous injection of such antimonials as antimony potassium tartrate and "diramin" (an aqueous solution of the products resulting from the reaction between antimony catechol and tris (hydroxymethyl) aminomethane in the presence of propylene glycol) to the intramuscular administration of the less toxic and more stable derivatives, such as lithium antimony thiomalate ("anthiomaline") and stibophen.[1]

In addition, adjuncts to antimony therapy have been advocated and appear to accelerate healing. These have included local application of various preparations such as oxidizing agents (potassium permanganate washes) or spirocheticidal substances as 10 per cent neoarsphenamine in equal parts of cod liver oil and glycerine.[1a] Other therapeutic measures have included the use of 20 per cent resin of podophyllum in olive oil applied for its escharotic activity on the granulation tissue, followed in turn by an epithelial stimulant such as scarlet red.[2] These additive measures, together with surgical treatment and irradiation, have often been necessary in the form of supplementary treatment to control the superimposed infection. The effectiveness of the employed therapeutic regimens when used either alone or in conjunction with one another decreases in direct proportion to the longevity of the lesion. The early lesions of granuloma inguinale respond well to therapy, and in rare instances ordinary hygienic measures may bring about a spontaneous cure.

It must be admitted that the antimonials will cause a regression and will result in abeyance of the disease in many patients with granuloma inguinale. However, a more rapid and propitious form of therapy was sought. The introduction of the various antibiotics led to their eventual trial in the management of this minor venereal disease. Thus, 1,000,000 to 2,000,000 units of penicillin has been administered to patients with no discernible benefit.[1c] Similar observations on the

This work was supported by a grant from the U. S. Public Health Service.

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Read before the Section on Dermatology and Syphilology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

1. (*a*) Greenblatt, R. B.: Management of Chancroid, Granuloma Inguinale and Lymphogranuloma Venereum in General Practice, Ven. Dis. Inform., 1943, supp. 19. (*b*) Paggi, L. C., and Hull, E.: Metastatic Granuloma Venereum: Report of a Case, Ann. Int. Med. **20**: 686-695 (April) 1944. (*c*) Greenblatt, R. B.; Deibert, A. V., and Fischer, S.: Treatment of Granuloma Inguinale with Diramin: A New Antimonial, J. Ven. Dis. Inform. **26**: 238-239 (Nov.) 1945. (*d*) Goldberg, L. C.: Treatment of Granuloma Inguinale with Anthiomaline: Report of Case with Extragenital Lesion, Am. J. Syph., Gonor. & Ven. Dis. **29**: 608-610 (Nov.) 1945.

2. Tomskey, G. C.; Vickery, G. W., and Getzoff, P. L.: The Successful Treatment of Granuloma Inguinale with Special Reference to the Use of Podophyllin, J. Urol. **48**: 401-406 (Oct.) 1942.

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refractoriness of granuloma inguinale to penicillin have been reported in the literature.[3] In contradistinction to the clinical observations with penicillin, in vitro studies have shown that penicillin in high concentrations was not without effect on the Donovan body.[4] It has also been shown that the local application of tyrothricin to the exuberant tissue characterizing many lesions of this disease failed to exert any appreciable therapeutic effect.[5] However, the eventual trial of streptomycin in contrast to the foregoing antibiotics has yielded the most promising outlook for the control of granuloma inguinale. Observations on the use and effectiveness of streptomycin in the treatment of granuloma inguinale have been presented in a preliminary report.[6] In this paper our observations on streptomycin are extended and a more detailed description of the cases is presented.

PATIENTS

A total of 48 patients have received streptomycin for granuloma inguinale. There was a total of 32 male and 16 female patients, all Negroes and ranging in age from 19 to 70 years. Of these 48 patients, 35 had received some form of antimony therapy for periods of time varying from one month to ten years. Most of these patients had received inadequate treatment at sporadic intervals. Some reported cures or disappearance of the lesion for short periods of time following antimony therapy. However, despite the duration of previous treatment with antimony compounds, Donovan bodies were demonstrated either by spread or biopsy section from the lesions of all patients before initiation of streptomycin therapy. The remaining patients who had not received previous antimony treatment had been given other forms of therapy such as penicillin, arsenic, or one or another of the sulfonamide drugs because of faulty diagnosis.

DOSAGE

The dosage of streptomycin employed ranged from 3.3 Gm. to 60 Gm. with an average dose of 20 Gm. The drug was given in amounts varying from 0.3 Gm. to 4 Gm. per day in divided doses every four hours for a period ranging from five to sixty-two days. The drug was dissolved in sterile distilled water containing 25 to 30 per cent of 1 per cent solution of procaine hydrochloride. In the earlier stages of this study the dose was judged empirically and was based on the extent and duration of the lesion. However, the present plan has entailed the administration of 4 Gm. of streptomycin per day for a period of five days. The purpose of this mode of therapy was twofold in nature: (1) to provide for a rapid and effective method of treatment and (2) to administer high doses and maintain high levels of streptomycin in the patient, thereby preventing the development of organisms resistant or refractory to the antibiotic.

TOXIC EFFECTS

Toxic reactions were noticed in 4 patients receiving daily doses of 1 to 4 Gm. of streptomycin. However, in no case was involvement of the eighth nerve observed. Pruritus was observed in all 4 cases, and in 1 patient this was associated with an urticarial eruption on the chest and extremities and a vesicular perioral dermatitis. Fifty milligrams of diphenhydramine hydrochloride, given twice a day, effectively controlled the pruritus in the 3 patients without the dermatitis, thereby permitting continuation of the streptomycin therapy. However, the patient exhibiting the dermatitis failed to respond to the same dose of diphenhydramine hydrochloride, and streptomycin therapy was advisedly discontinued. A fifth patient complained of a mild burning of the conjunctiva after having received a total dose of 3 Gm. of streptomycin over a ten day period. Administration of the drug was discontinued for four days, and with resumption of the same dose no untoward symptoms were noticed.

RESPONSE AND CLINICAL EFFECT

Frequent smears were taken from the lesions of the patients receiving streptomycin throughout the course of treatment. Negative smears were obtained within two to eleven days, or an average of six days (in 26 patients), after initiation of the streptomycin injections. However, the lesions clinically still showed evidence of granulation tissue. Microscopically it was observed that the streptomycin apparently caused disintegration of the Donovan bodies. On the other hand, we have frequently observed well preserved Donovan bodies in smears of the lesions in patients who have received stibophen two times weekly for several months. Donovan bodies were observed in the lesions of these patients despite the evidence of decided clinical improvement. The significance of these observations will be discussed later, and a more detailed account will be presented elsewhere in a report devoted to bacteriologic aspects of this problem. The patients treated with 0.3 to 1 Gm. of streptomycin per day were maintained on the antibiotic until few or no residual lesions were observed. However, the patients treated for five days with 4.0 Gm. of the drug per day still showed granulomatous lesions at the time that the streptomycin therapy was discontinued. Nevertheless, despite the lack of additional therapy, the lesions in these patients eventually showed complete healing, eight to twelve days after cessation of treatment. All the patients, especially those with extensive lesions, volunteered the information that within twenty-four to thirty-six hours after initiation of streptomycin therapy the pain or discomfort associated with the lesion was markedly reduced or absent. Some healing of the lesions was noted within twenty-four to forty-eight hours after the antibiotic had been administered. Healing was, at first, centripetal in nature.

Streptomycin in the Management of Granuloma Inguinale

Sex of Patient	No. of Patients	Average Total Dose, Gm.	Length of Treatment, Days	Healing After Therapy, Weeks	Follow-Up Study	
					Percentage	Weeks
Male.....	33	19.3 (3.6-60)*	14.6	2.9	63.7	9.1
Female.....	15	21.8 (3.3-94)	16.8	3.4	80.0	7.5
Total.....	48	20.2	16.5	3.0	69.8	8.5

* Figures in parentheses indicate dose range employed.

RELAPSES

Since the inception of this study has been of relatively recent origin the follow-up studies have been, of necessity, short in duration. To date there have been three

3. Haserick, J. R.: Failure of Penicillin in Treatment of Granuloma Inguinale: Report of a Case, Arch. Dermat. & Syph. **52**: 182 (Sept.) 1945. Turner, F. B.: Treatment of Seven Cases of Granuloma Inguinale with Penicillin, M. J. Australia **2**: 366-367 (Dec. 1) 1945.
4. Beveridge, W. I. B.: The Action of Antimony and Some Other Bacteriostatic Substances on Donovania Granulomatis Isolated in the Chick Embryo, J. Immunol. **53**: 215-223 (July) 1946.
5. Greenblatt, R. B., and Kupperman, H. S.: Unpublished data.
6. Greenblatt, R. B.; Kupperman, H. S., and Dienst, R. B.: Streptomycin in the Therapy of Granuloma Inguinale, Proc. Soc. Exper. Biol. & Med. **64**: 389-390 (April) 1947.

recurrences after therapy had been discontinued. Two of these patients had received less than 4 Gm. and 1 had received a total dose of 28 Gm. The lesion of this latter patient was almost completely healed, and after dismissal further healing occurred. However, there was a recrudescence of the lesion three

Fig. 1 (J. A.).—Granuloma inguinale of six years' duration in the genital area of patient. Note general destruction of genitalia by extensive granulation tissue.

months later. A second course of streptomycin therapy (1.5 Gm. per day for forty-one days followed by 4 Gm. per day for nine days or a total dose of 94 Gm. of streptomycin) was administered over a period of fifty

Fig. 2 (J. A.).—Granulomatous involvement of medial portion of left thigh and perianal area by extension of granuloma inguinale from the genital region.

days. Since no further progress toward healing occurred, it was concluded that the disease had become refractory to the antibiotic. Lithium antimony thiomalate therapy was then instituted in doses of 3 cc. injected intramuscularly six times a week for four weeks. Complete healing occurred with a total dose of 72 cc. Follow-up studies in the patient are still in progress. She is to receive 3 cc. of lithium antimony thiomalate twice weekly for the next few months to prevent any further recurrence. Of the other 2 patients showing relapses after an initial course of therapy of less than 4 Gm. of streptomycin, recrudescence of the disease was noted within eight weeks after discontinuing the injection of the antibiotic. One patient received an additional course of treatment consisting of 4 Gm. of streptomycin per day given for eleven days. The lesion healed completely and there has been no evidence of a recurrence five weeks later. The other patient was also placed on 4 Gm. of streptomycin per day for eight days. Healing has occurred and the patient is now under observation.

REPORT OF CASES

Case 1.—J. A., a Negro man 31 years of age, first noticed a lesion on the glans penis in 1941, six years before the present admission. The patient received a course of intravenous injec-

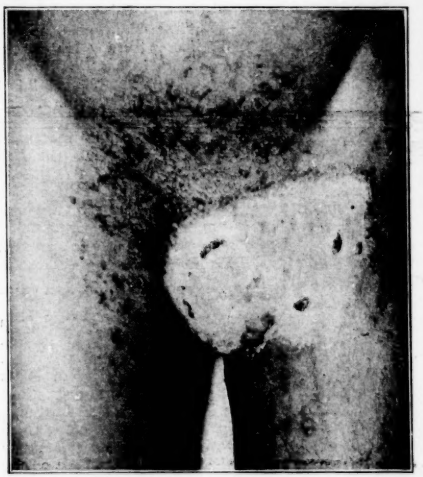

Fig. 3 (J. A.).—Healed genital area three weeks after cessation of streptomycin therapy (cf. fig. 1).

tions at this time and some healing occurred. However, with further treatment the lesion continued to spread and heal alternately, so that eventually as a result of scar formation the penis was completely retracted and could not be recognized. Soon after the appearance of the penile lesion a pustule appeared in the suprapubic area. This area ulcerated and coalesced with the penile lesion to involve the genital region, medial aspect of the left thigh and the perineum. Despite intermittent antimony, arsenic and bismuth therapy the lesions slowly spread to their present proportions.

Examination showed a well developed poorly nourished Negro in apparent distress who could stand in the erect posture only with difficulty. A foul, acrid odor was associated with an extensive granulomatous lesion in the genital area (fig. 1). The lesions were extensive and characterized by a moderately proliferated red granulating base covered with a weeping, serosanguinous grayish exudate. There were no visible external genitalia, and the urinary meatus was camouflaged by the surrounding ulcerated area and could not be identified. The lesion involved the suprapubic area and left inguinal region, and extended down the medial aspect of the thigh to the perineum and perianal area (fig. 2). Smears made from the

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lesions showed numerous Donovan bodies. The penis and scrotum while not apparent were covered by the granulation tissue (fig. 1). The patient was placed on 1 Gm. of streptomycin per day, administered in divided doses at four hour intervals. Smears made on subsequent days showed Donovan bodies in the lesion to be present only for the first five days

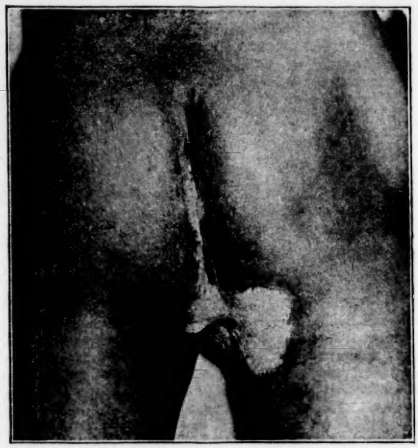

Fig. 4 (J. A.).—Healed perianal and perineal lesion observed after cessation of streptomycin therapy (cf. fig. 2).

of streptomycin therapy. Thereafter negative smears were obtained. The pain associated with the lesion was markedly reduced after the first day of treatment and completely absent after forty-eight hours. The patient received a total dose of 21 Gm. of streptomycin. At the time that the injections were discontinued small areas of granulation tissue were present. These were completely healed three weeks after cessation of streptomycin therapy (figs. 3 and 4). No recurrence has been observed sixteen weeks after treatment. After the streptomycin therapy had been discontinued the urinary meatus could then be seen in the healed area between the medial left thigh and inferior lateral portion of the infrapubic area (fig. 3). Future plastic surgery has been advised for repair and proper presentation of the penis and scrotum.

CASE 2.—L. M. F., a Negro woman 26 years of age, was admitted to the granuloma ward because of extensive lesions and scar formation of the pubic and perineal area. The initial lesion was noticed six years ago in the left inguinal region. The lesion spread from this area to the suprapubic region and by retrograde extension to the vulva and perineum. These areas were all at one time involved with the granulomatous lesion characterizing the patient's disease. She had received intermittent antimony therapy at different clinics over the last six years and, while improvement of the lesion was noticed, complete healing never was attained.

Examination showed a well developed and well nourished Negro woman exhibiting extensive scar formation and depigmentation in the inguinal and genital region. Granulation tissue was observed in one small lesion in the right suprapubic region extending down on the right labium majus to the perineum and perianal area with some extension up the inferior part of the left labium majus. There was marked depigmentation of both labia associated with elephantiasic enlargement of a brawny indurated nature. Smears made from the lesion showed numerous Donovan bodies to be present. The patient was placed on 0.3 Gm. of streptomycin per day for twenty-six days, or a total dose of 7.8 Gm. Healing was apparent after 2 Gm. had been administered. Complete healing was present when the patient had received the total dose. Follow-up study of ten weeks has shown no recurrence.

CASE 3.—R. A., a Negro man 22 years of age, had noticed a small nodular swelling of the glans penis five years prior to his present admission. This lesion ulcerated and gradually involved the entire glans and the distal portion of the shaft. Soon after the development of the penile lesion similar ulcers appeared first in the right and then in the left inguinal region. The ulcerated areas became confluent by direct extension and spread inferiorly to the perineum and perianal area so that at one time the genital, inguinal and perianal areas were one beefy red mass of granulation tissue. In addition, circular contact lesions developed on the medial aspect of each thigh. Soon after the beginning of the penile ulcers the patient was placed on antimony potassium tartrate, and finally stibophen was administered intermittently from 1942 to the present date. The antimony therapy induced sporadic healing in some sites with resulting scar and keloid formation. However, at no time were all lesions completely healed.

Examination revealed a well developed, poorly nourished Negro man in apparent distress and emitting a foul, pungent odor. There were extensive keloid formation and depigmentation in both the inguinal and pubic regions. The penis could not be recognized and was represented by a small tuft of granulomatous tissue pointing toward the left thigh. A linear mass of granulation tissue extended from the left inguinal region to the perineum. A circular contact granulomatous lesion was present on the medial aspect of the left thigh in an area where healing had previously occurred (fig. 5). There was also an area of granulation tissue on the right side between thigh and scrotum (fig. 5). The scrotum was completely retracted by keloid formation and the testis was pressed against the external abdominal ring. The ulcerated areas showed the typical granulomatous lesions characterizing granuloma inguinale. There was a small amount of superficial exudate on the typical

Fig. 5 (R. A.).—Active granuloma inguinale infection of genital area associated with erosion of penis.

beefy red granular base. Numerous Donovan bodies were demonstrated in spreads from the lesions The patient was placed on 4 Gm. of streptomycin per day for a total dose of 20 Gm. The pain associated with the lesion was alleviated within twenty-four hours after the streptomycin injections had been initiated. Healing was evident within forty-eight hours and Donovan bodies could not be demonstrated in spreads made

from the lesion after the patient had received 16 Gm. of streptomycin over a four day interval. After cessation of injections appreciable granulation tissue was still evident. However, three weeks later complete healing had occurred, with only a small area of granulation tissue present at the region of the external urinary meatus (fig. 6).

CONCLUSIONS

1. Streptomycin was employed in the management of 48 cases of granuloma inguinale in doses ranging from 3.3 to 60 Gm., administered over a period of time ranging from five to sixty-two days. Healing occurred in all patients, either while the antibiotic was being administered or after cessation of therapy.

An average follow-up study of nine weeks has shown that the disease recurred in 3 patients; of these, 2 responded to a second course of therapy. In the third patient resistance to the drug developed; she was placed on an organic antimony compound. Some patients

Fig. 6 (R. A.).—Healed lesion seen three weeks after cessation of streptomycin therapy (cf. fig. 5).

have shown no recrudescence of the lesions four to five months after cessation of therapy.

A five day treatment schedule has been evolved. This is based on the administration of 4 Gm. of streptomycin per day or a total dose of 20 Gm. of the antibiotic over the five day period. Lesions were present after this therapy had been discontinued, but complete healing occurred within the next one to four weeks despite the fact that no additional drug was given.

The only toxic effects noted after administration of streptomycin were pruritus (4 cases) and urticarial dermatitis (1 case). No involvement of the eighth nerve was observed. The pruritus was controlled in 3 patients by the administration of diphenhydramine hydrochloride.

It is concluded that streptomycin gives promise of being the most effective drug in the control of granuloma inguinale and that only longer post-treatment periods of observation are necessary to establish this contention.

ADDENDUM

Since the presentation of this paper, an additional 43 patients have been treated with streptomycin, bringing the total to 91 cases. Analyses of the results of the complete series now show that of the 32 patients who received 2 Gm. per day or less of streptomycin over a period averaging twenty days there were 8 recurrences, 7 of which were retreated, with successful results in 5. The remaining 2 have become streptomycin resistant. Of the 51 patients treated with 4 Gm. per day for five days, there has been 1 recurrence which healed with retreatment. Seven patients received 4 Gm. per day for more than five days, i. e., six to ten days, with no relapses thus far. One patient was treated with streptomycin vaginal suppositories alone, 4 Gm. per day for four days, with complete healing. From our data, it appears that the administration of 4 Gm. of the drug per day for five days is the most satisfactory as well as the most economical method of treatment.

ABSTRACT OF DISCUSSION

Dr. Robert R. Kierland, Rochester, Minn.: The results obtained by the authors are far superior to those obtained by any previous method of therapy available for this chronic and disabling disease. So outstanding are their figures that one may be tempted to use streptomycin as a "therapeutic trial" in cases of unproved but strongly suspected granuloma inguinale. These findings confirm or are confirmed by the independent investigation made by Barton and his associates (Barton, R. L.; Craig, R. M.; Schwemlein, G. X., and Bauer, T. J.: Granuloma Inguinale Treated with Streptomycin: Report of Three Cases, unpublished data) at the Chicago Intensive Treatment Center, the results of which were submitted for publication in September 1946. Their original series comprised 3 patients but they have since added more. The first 3 patients with proved granuloma inguinale received 20,000 to 30,000 units of streptomycin every three hours until a total dosage of 4,000,000 to 7,000,000 units had been received. There was evidence of rapid clinical improvement, while Donovan bodies could not be found in scrapings of tissue as early as ten days after treatment. Relapses occurred in 2 of these patients. Later, however, in 7 additional patients (Marshak, L. C.; Barton, R. L., and Bauer, T. J.: Granuloma Inguinale: A Report of the Literature and a Report of Ninety-Seven Cases with a Note on Streptomycin Therapy, unpublished data), the dose per injection was increased to 50,000 units and a total dosage of 6,000,000 to 10,000,000 units was given with no relapse as long as six months after treatment. It is entirely possible that the use of large doses of 4 Gm. daily for five days, advocated by the present authors, has added materially to the small incidence of relapse. The factors of optimal dosage, duration of treatment and the combination of streptomycin with other therapeutic agents will undoubtedly be determined in the future. The relative purity of streptomycin is a matter that has received much discussion as far as reactions are concerned. As purer forms of the drug are obtained the incidence of cutaneous reactions may be lowered. The appearance of the more serious toxic manifestations, such as nerve deafness and loss of labyrinthine function, may be due to the drug itself and is an indication for discontinuance of the drug. That this will be unusual is indicated by the fact that no serious toxic reaction occurred in this series of 48 cases. The original demonstration of the culture and propagation of Donovania granulomatis by Anderson and more recently by others leads the way for the in vitro investigation of streptomycin and other antibiotic substances.

Dr. Donald M. Pillsbury, Philadelphia: This is the type of paper on which discussion is a pleasure, because the authors are competent observers, ha e maintained adequate and expert laboratory controls on the clinical diagnosis, report a significant

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number of patients treated and are conservative in their statements of the results obtained. There seems no question that streptomycin in moderate doses has a strikingly favorable effect on the lesions of granuloma inguinale in most patients with this disease. Moreover, although the average time of follow-up observation in the authors' 48 patients is only nine weeks, it seems most probable that a majority of those treated have been cured. Certainly the results achieved are much superior even to those obtained with intensive daily stibophen therapy. Any one who has been associated for some years with a large clinic for venereal or dermatologic diseases inevitably comes to the conclusion that granuloma inguinale is one of the worst treated of all the diseases affecting the skin and subcutaneous tissues. The unfortunate patients with this disease are ordinarily not blessed with even average intelligence, and continuous treatment and adequate follow-up of them are difficult to accomplish. Furthermore, the lesions of the disease lack esthetic appeal to say the least, and few physicians and nurses will carry out the necessary diagnostic and local procedures with any enthusiasm. As a result, one regularly sees patients who have had intermittent treatment and who have drifted from one clinic to another, with increasing disability, mutilation and discomfort from the disease. Streptomycin therapy offers hope that most of these patients can be cured within a short period of treatment. Fortunately, the amounts of streptomycin which seem necessary are not of an order likely to produce a high incidence of serious reactions. The calculated risk is well justified. It must be kept in mind that streptomycin when administered over periods of weeks to months, is capable of producing severe reactions and permanent disability. In a study recently completed under the auspices of the Streptomycin Committee of the Veterans' Administration, and in other studies, it has been found that streptomycin may have definite toxic effects on the vestibular and/or acoustic portions of the eighth nerve, with a possibility of total deafness if the drug is continued, may produce irreversible renal damage, rarely may produce dermatitis reactions of the ninth day erythema type and, also rarely, may have dangerous effects on bone marrow function.

DR. HAROLD L. HIRSH, Washington, D. C.: Early this year we learned about the work of Dr. Kupperman and his associates and consequently undertook a study of the treatment of granuloma inguinale with streptomycin. We have completed the treatment of 17 patients. We used a total of 1 Gm. a day given intramuscularly in divided doses every four hours. Our results are almost identical with those reported by Dr. Kupperman and his associates. We, too, noted that within twenty-four or forty-eight hours there was marked relief in the pain from the lesions. Particularly the female patients who previously refused to allow examination were quite willing to be examined. Furthermore, the lesions which had previously been red and raw and angry in appearance became less intense, purplish in color and showed evidence of healing. In about a week, it was evident that the lesions were healing in a centripetal fashion. Although some of these patients had extensive granulomatous masses, at about the end of a week the masses began to shrink in size and the shrinkage continued even after treatment was discontinued. In several patients we contemplated removing these extensive granulomatous masses after treatment was completed. This was done on only 1 male patient for the purpose of examining the residual tissue more completely. We only did weekly smears and found that in every patient the Donovan bodies were present at the end of one week; in the second week specimens they were completely gone. The duration of treatment in our patients has ranged from eight to forty-seven days. We continued treatment until the ulcerative lesions were completely healed. The follow-up period has now been for periods up to ten weeks for some patients. We noticed that in patients who had moist ulcerative lesions that were in apposition or that were bathed by vaginal discharge the healing was somewhat slower. We had several complications in our series. One patient was delivered of a viable infant at seven months, ten days after treatment was started. Another patient was six months pregnant when treatment was started and at the conclusion of treatment her pregnancy had apparently progressed uneventfully. Another patient had secondary syphilis which was treated with penicillin concurrently with apparently good results. Another interesting problem was that 1 of the patients with a granulomatous lesion of the groin had a remarkable response for the first ten days, but thereafter there was no further improvement. We went back and studied the original and follow-up slides and found that he also had a squamous cell carcinoma at the site of the venereal disease. We think that the effect of streptomycin in granuloma inguinale is remarkable.

DR. HARRY M. ROBINSON, Baltimore, Md.: It would be a great satisfaction to get a good result in some of those poor suffering Negroes who in the vast majority of instances have no money and no facilities for treatment and for whom hospitalization is practically impossible to obtain. I did not hear whether the investigators made any biopsies from the scars. In some of those patients whom we treated with other methods, in doing biopsies on scars we found cells including Donovan bodies. We were able to control granuloma inguinale to a certain extent with the antimony products when the condition was caught in the early stage, but when the treatment was stopped, later practically the entire condition recurred. In some of the patients on whom we worked with excision, while some of the scar following excision remained undisturbed, at the margin of the scar new granuloma inguinale tissue appeared. I certainly hope that this bears out the promise that it appears to have. I am not saying this in a questioning mood; it is just a marvelous possibility, and we hope to try it ourselves.

DR. R. B. GREENBLATT, Augusta, Ga.: Through the Public Health Service we were able to obtain supplies of streptomycin, and work on a series of cases was started in the early fall of last year. Of all the diseases which we see in the South, granuloma inguinale is one of the tragic illnesses. The wretched, poverty-stricken patients do poorly on ambulatory treatment with antimonials, and some cases have come to our attention in which foul, ulcerative wounds have been present for ten to twelve years. Dr. Kierland made mention of the Chicago group who last summer treated 3 cases. We are glad to hear about it and would like to concede priority to them. We did not know about their experimental work at the time that we made our contacts for work with streptomycin in granuloma inguinale. Dr. Pillsbury's remark that "we owe a debt to society in the treatment of patients with granuloma inguinale" is timely. We, too, feel that though these patients have to be hospitalized and though streptomycin is expensive we can at least offer them hope for rehabilitation and an opportunity to become decent members of society. Heretofore, I think the management of granuloma inguinale has been a blot on our public health escutcheon. The apathy shown by physicians in the care of these patients is regrettable. Dr. Hirsh, we are happy to learn, has been able to corroborate our findings on the use of streptomycin. We are pleased to hear that he has developed a medium in which streptomycin may be administered at daily intervals. In regard to Dr. Robinson's query on whether biopsies were obtained from scar tissue, I might say that in all patients in this series biopsies or smears were taken before therapy and for many weeks after therapy. In only 1 instance was a biopsy taken from a healed scar to see whether Donovan bodies were to be found deep in the tissues. In the sclerosing type of granuloma inguinale a presumably spontaneous healing takes place by scar tissue. However, the study of biopsy sections from these scars reveals the presence of Donovan bodies. After adequate streptomycin therapy Donovan bodies disappear rather rapidly, and though healing may take place comparatively slowly, the granulation tissue remains free from the Donovan body until healing is complete.

EFFECTS OF URETHANE IN THE TREATMENT OF LEUKEMIA AND METASTATIC MALIGNANT TUMORS

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The results in the treatment of chronic leukemia with urethane (ethyl carbamate), reported by Paterson, Haddow, ApThomas and Watkinson,[1] were sufficiently promising to stimulate further clinical investigation of this drug. We are presenting a report of our observations of the effect of urethane on leukemia and some of the malignant neoplastic diseases.

Urethane ($H_2N.CO.OC_2H_5$) was first synthesized by Dumas[2] in 1834 from ethyl chloroformate and ammonia. White crystals are formed which are readily soluble in water and many of the commonly used organic solvents. It belongs to a group of organic esters of carbamic acid which are known collectively as urethanes because of their structural similarity to urea. The term "urethane" has been generally applied to ethyl carbamate itself. Carbamic acid is unstable and has not been isolated in the free state.

Although an extensive literature concerning urethane exists there are many gaps in our knowledge relative to its pharmacologic actions. Schmiedeberg[3] studied its narcotic property in dogs and noted that with anesthetic and sublethal doses there was no significant effect on the pulse and respiration. Jolly[4] was apparently the first to note the effectiveness of urethane as a hypnotic in clinical medicine. A number of other favorable publications appeared toward the end of the nineteenth century.[5] The drug was popular for a brief period, but because of its weak and uncertain hypnotic action it was soon replaced by the more dependable barbiturates, then being introduced.

Haddow and Sexton[6] have reviewed the experimental work leading up to the trial of urethane in the treatment of malignant growths and the incidental discovery that it was more effective in inducing remissions in human leukemia. Recent reports[7] confirm the effectiveness of the drug in mouse myelogenous and rat lymphatic leukemia. In this regard attention should be directed to the study of Hawkins and Murphy[8] in 1925 on the effect of urethane in normal rabbits and rats. They found that urethane induced relative lymphocytopenia and granulocytosis, which they attributed to an accompanying uncompensated alkalosis. They obtained similar results by the injection of sodium bicarbonate or the administration of toxic doses of roentgen radiation. In addition they noted that rats under urethane anesthesia, given an exposure to roentgen rays well below the lethal dose, invariably died within seven to fourteen days.

Other effects reported with urethane include a decided antibacterial action,[9] a significant antihistamine action which has been applied to the symptomatic treatment of bronchial asthma;[10] hyperglycemia and glycosuria;[11] azotemia and increased urinary nitrogen excretion;[12] parasympatholytic effect;[13] toxicity for rat liver,[14] and carcinogenic action on mouse and rat lung[15] and rat liver.[15b] From its narcotic action it appears that the drug is rapidly absorbed from the gastrointestinal tract and rapidly eliminated from or altered in the body. That urethane is converted to urea and carbon dioxide in the body[16] is no longer believed to be likely.[17]

METHOD OF ADMINISTRATION

Urethane was administered in several ways. Paterson and co-workers[1] prescribed the drug in a solution of chloroform water and syrup of orange. We have used 0.5 Gm. gelatin capsules and 0.5 Gm. enteric-coated capsules.[18] Forty and 50 per cent solutions were used for intramuscular injection in some patients. Nausea was occasionally complained of soon after the nonenteric-coated capsules were ingested. We attribute this nausea to gastric irritation. Nausea with vomiting rarely developed after two or three weeks of oral therapy. This delayed nausea, which was prominent in case 15 during the third course of urethane, occurred after the dose had been doubled to 2 Gm. three times a day for ten days. Enteric-coated capsules were being given at this time. It is possible that this delayed nausea is a sign of overdosage. As much as 2 Gm. three times a day has been given intramuscularly without any complaint of local irritation. A hypnotic effect characterized by dizziness and drowsiness was fre-

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Read before the Section on Internal Medicine at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

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quently noticed when urethane was given intramuscularly. A slight sedative effect was noticed by the patients taking 1 Gm. three times a day by mouth. We have not noticed any toxic effects other than nausea and occasional vomiting.

TREATMENT OF LEUKEMIA

The table is a summary of the essential clinical data obtained in the study of 25 patients with leukemia and lymphomatous diseases. It is noteworthy that the patients with acute and subacute leukemia died after

Summary of Essential Clinical Data in Twenty-Five Cases of Leukemia and Lymphomatous Diseases

Case No. and Patient	Sex	Age	Diagnosis	Therapeutic Decrease in Leukocytes	Morphologic Changes of Blood	Decrease in Size of Spleen and Lymph Nodes	Urethane Administration	Tolerance of Urethane	Clinical Result
Acute and Subacute Leukemia									
1 L. J.	M	28	Acute lymphatic	29,800 to 750	10% reduction in lymphoblasts	Slight	1 Gm. t. i. d. oral capsules	Fair, slight nausea	3 day slight remission; died after 17 days
2 A. S.	M	36	Acute lymphatic	7,300 to 550	Slight reduction in lymphoblasts	None	1 Gm. t. i. d. oral capsules	Fair, slight nausea	Downward course; died after 18 days
3 W. S.	M	57	Acute lymphatic	6,200 to 4,100; subsequently rose to 22,000	Slight reduction in lymphoblasts	Slight	1 Gm. t. i. d. oral capsules	Good	Alive after 6 weeks; condition stationary
4 S. S.	M	64	Acute monocytic	8,700 to 2,650	No change	None	1 Gm. t. i. d. oral capsules	Good	Downward course; died after 21 days
5 C. T.	F	58	Acute myelogenous	71,000 to 6,450	Maturation noticed	Slight	1 to 2 Gm. t. i. d., oral capsules-roentgen therapy	Good	Downward course; moderate remission; died after 65 days
6 E. F.	M	37	Acute myelogenous	322,000 to 122,000	None	None	1 Gm. t. i. d. oral enteric-coated capsules and plain capsules	Good	Rapid downward course; white blood cells elevated after discontinuing urethane
7 G. R.	M	53	Subacute myelogenous	74,500 to 400	None	None	1 Gm. t. i. d. oral enteric-coated capsules; total dose only 12 Gm.	Good	Leukocytes remained below 5,000 until death; leukemia cutis developed; died 72 days after therapy was discontinued
8 B. S.	M	4	Subacute lymphatic	11,300 to 350	Almost complete reduction in lymphoblasts	Slight	0.25 Gm. daily to t. i. d., oral	Good	Good remission following treatment; duration of illness approximately 11 mo.; died
9 G. G.	F	44	Subacute lymphatic	155,200 to 16,000	None	None	1 Gm. t. i. d. oral capsules	Fair, nausea, loss of appetite	Downward course; central nervous system infiltration; leukemia cutis; died
Chronic Lymphatic Leukemia									
10 W. G.	M	47	Chronic lymphatic	228,000 to 1,800	Blood and marrow smears now seem to be normal	Moderate	1 Gm. t. i. d. oral capsules; 90 r therapy	Good; slight nausea	Excellent; no apparent evidence of leukemia in blood or marrow (6 mo.); spleen lymph nodes still palpable
11 M. V.	F	72	Chronic lymphatic	80,000 to 18,000	Decrease in lymphocytes	Slight	1 Gm. t. i. d. oral capsules	Poor; nausea	Fair; urethane better than roentgen rays
12 K. K.	M	60	Chronic lymphatic	230,000 to 80,000	None	Slight	1 to 2 Gm. t. i. d. oral capsules; 2 cc. 50% solution intramuscularly t. i. d.	Nausea; vomiting; dizzy after intramuscular therapy	Poor; died 3 weeks after subsequent roentgen therapy; leukemia of 5 years' duration
13 S. S.	M	58	Chronic lymphatic	321,000 to 90,000	None	None	1 Gm. t. i. d. oral capsules	Fair	Died suddenly after completion of therapy
14 H. B.	M	53	Chronic lymphatic	76,000 to 30,000	None	None	1 Gm. t. i. d. oral capsules given for 84 days	Good	Died
15 F. K.	M	57	Chronic lymphatic	188,000 to 55,000; 98,000	Slight reduction in lymphocytes	Moderate	1 Gm. t. i. d. plain oral capsules; then enteric-coated	Good	Fair; diminution in size of lymph nodes to one half; no change in spleen
16 W. H.	M	51	Chronic lymphatic	120,000 to 90,400	Less smudge cells	Slight	1 Gm. t. i. d. plain oral capsules	Good	Course of therapy not completed
17 W. Q.	M	72	Leukosarcoma	22,000 to 15,100	Slight reduction in lymphocytes	Complete reduction in spleen and lymph nodes	2 cc. 50% solution intramuscularly; t. i. d.; later enteric coated capsules	Good	Excellent; temporary remission
18 J. W.	M	57	Chronic lymphatic	65,000 to 43,000	None	Very slight	1 Gm. plain capsules t. i. d. for 1 mo.	Good	Slight improvement in well-being
Chronic Myelogenous Leukemia									
19 O. S.	M	57	Chronic myelogenous	340,000 to 3,400	Decrease in immature cells	Complete	1 to 2 Gm. t. i. d. plain and enteric-coated capsules; 2 to 4 cc. 50% solution intramuscularly	Good	Excellent
20 P. H.	F	49	Chronic myelogenous	190,000 to 8,000	Decrease in immature cells	Complete	1 Gm. t. i. d. plain and enteric-coated capsules	Good	Excellent
21 D. H.	M	68	Chronic myelogenous	125,000 to 8,200	Decrease in immature cells	Slight	1 Gm. t. i. d. plain capsules	Good	Good
22 J. P.	M	57	Chronic myelogenous	57,000 to 20,000	Slight decrease in immature cells	No splenomegaly present	1 Gm. t. i. d. enteric-coated capsules	Good	Good; had received roentgen therapy 6 mo. previously; recurring weakness and fatigue relieved by urethane
Lymphomatous Diseases									
23 R. D.	M	39	Giant follicle lymphoma	13,600 to 7,600	None atypical lymphocytes	None	1 Gm. t. i. d. plain capsules	Slight nausea and anorexia	Unsatisfactory
24 A. K.	F	39	Hodgkin's disease	13,600 to 8,950	None	None	1 Gm. t. i. d. plain capsules	Good	Unsatisfactory
25 R. C.	M	28	Hodgkin's disease	6,000 to 1,900	None	None	1 Gm. t. i. d. plain capsules	Poor	Unsatisfactory

a period of time comparable to that observed in patients treated by other therapeutic measures or without any treatment at all. Even though the number of leukocytes fell to severe leukopenic levels in most instances, the patients progressed along a more or less uninterrupted downhill course. In 2 of these patients, 7 and

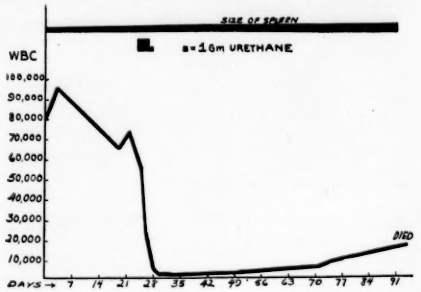

Fig. 1.—Clinical course in case 7 (subacute myelogenous leukemia and leukemia cutis).

9, a severe degree of leukemia cutis developed during and after the taking of urethane, even though their leukocyte counts were lower than before the institution of therapy (fig. 1). Patient 5 received a combination of urethane and roentgen therapy. Two courses of roentgen therapy (330 r and 440 r) were given with an interval of one month. Urethane was administered immediately after the second course of roentgen therapy, which, incidentally, had been applied to the mouth, the site of extensive leukemic infiltration. The leukocyte count eventually rose to 85,000 at the time of the patient's death, even though urethane was being received. Autopsies were performed in cases 1, 2 and 5. Extensive leukemic involvement of the marrow and other organs was found.

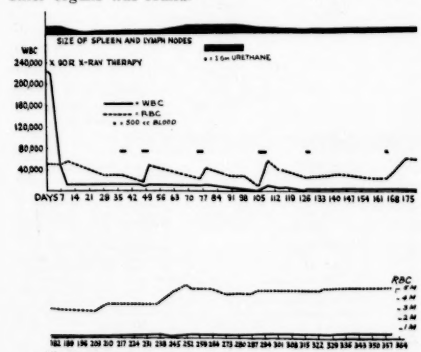

Fig. 2.—Clinical course in case 10 (chronic lymphatic leukemia).

Results have been more favorable in the chronic lymphatic group. Of the 8 patients treated, 3 have died.

One of these, patient 13, a Negro, had been ill for five months. He had extensive lymphadenopathy and splenomegaly when first seen. Hypertensive heart disease was also present. Urethane was administered for thirty days. During this time his leukocyte count fell to a low level of 117,500. His spleen and lymph nodes decreased only slightly in size. He died suddenly on the forty-fourth day. At this time his leukocyte count was 96,000. An autopsy was not performed and the exact cause of his death was not ascertained.

Case 14 was considered to be a more acute form of chronic lymphatic leukemia. This patient was admitted to the hospital with hemiplegia on the right side which had developed suddenly two weeks previously. He had been in apparent good health until that time. The sternal marrow was heavily infiltrated with lymphoblasts and lymphocytes with numerous cytoplasmic vacuoles. He was given urethane for fifty-two days without any improvement. Death occurred fifty-eight days after urethane therapy had been instituted. This is the only case in the series in which neither clinical nor hematologic change was observed.

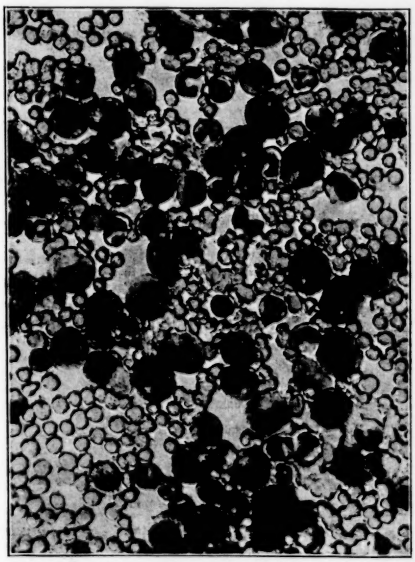

Fig. 3.—Sternal marrow before urethane therapy in case 19 (chronic myelogenous leukemia).

Patient 10 (fig. 2) initially received 90 r of roentgen therapy to his spleen in May 1946. His leukocyte count fell from 228,000 to 12,000 with this small amount of therapy. There was only a slight decrease in the size of the lymph nodes and spleen, however, and he continued to become weak and more anemic. Six blood transfusions (500 cc. each) were given during the following nine weeks. His leukocyte count remained between 8,200 and 12,400, with from 73 to 69 per cent lymphocytes. He was given potassium arsenite solution for two days but could not tolerate the drug because of nausea and diarrhea. He was rehospitalized in July 1946, given three blood transfusions for his refractory anemia and started on a course of 3 Gm. of urethane a day. After eighteen days his leukocytes fell to 1,200 and his erythrocytes to 560,000. Administration of urethane was discontinued, multiple blood transfusions were given, and he gradually improved. After six weeks his sternal marrow smears showed a pronounced decrease in lymphocytic infiltration and an increase in erythropoiesis. The differential blood counts began to show a reduction in lymphocytes. Since Jan. 6, 1947 his erythrocyte and leukocyte counts have been essentially normal. It is impossible to diagnose leukemia from

19. Footnote deleted in proof.

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an examination of his blood and bone marrow. Splenomegaly and inguinal and axillary lymphadenopathy have remained relatively unchanged. This patient has returned to work entirely free from symptoms.

In the remaining cases of chronic lymphatic leukemia there has been fairly good response to urethane therapy. Patient 11 stated that she felt better after a course of urethane than after roentgen therapy. Her spleen diminished in size. Patient 12 had also been previously treated with roentgen rays. Urethane alone, given orally and intramuscularly for forty days, failed to produce a remission. He was given 1,092 r along with urethane, and a remission was promptly induced. This patient died suddenly after what appeared to be an acute myocardial infarction three weeks later. Cases 15

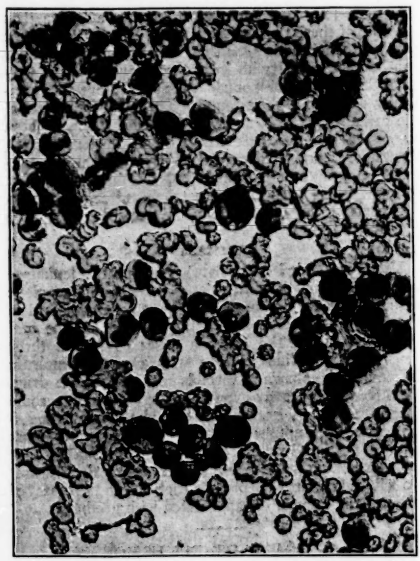

Fig. 4.—Sternal marrow after urethane therapy in case 19. Myeloblasts and premyelocytes have given way to more mature cells.

and 18 are early benign cases. These patients have experienced some hematologic and clinical improvement.

In each of the 4 cases of chronic myelogenous leukemia there has been good response to urethane. Splenomegaly was reduced and fatigability, diaphoresis and headache, when present, disappeared usually after a week of treatment. The leukocyte count approached normal and sternal marrow and blood smears revealed a noticeable change toward maturity (figs. 3 and 4). Patient 19 has had chronic myelogenous leukemia for two and one-half years. Three remissions have been induced (fig. 5). This patient prefers urethane therapy to roentgen therapy which he had previously received in 1945. In the remaining 3 cases there have been similar favorable responses. The fall in leukocyte count may be abrupt or gradual. This fall usually continues after administration of urethane is discontinued. Our results in chronic leukemia are comparable to those of Paterson and her co-workers [1] and others.[20]

Two patients with Hodgkin's disease have not been benefited by urethane. In case 19 leukopenia developed after six days of therapy. This patient was transferred to another hospital for more roentgen therapy. Patient

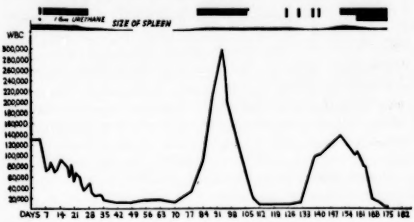

Fig. 5.—Clinical course in case 19.

18, whose disease is refractory to roentgen rays after intensive therapy, failed to show any improvement with thirty days of treatment. She was subsequently given a course of nitrogen mustard therapy and went into a relatively satisfactory remission. Case 21, giant follicle lymphoma, was not improved by twenty-one days of therapy, although a decrease in lymphocytes was noticed. This patient has recently received nitrogen mustard with a rather satisfactory result. In case 20, leukosarcoma with extensive lymphadenopathy, there was good response at first to intramuscular administration of urethane, 2 Gm. three times a day for fifteen days. Lymphadenopathy almost vanished and the symptoms disappeared. Three weeks later weakness and nausea returned. The patient was given urethane orally, 3 Gm. a day for fourteen days, and again felt much improved.

EFFECT ON MALIGNANT NEOPLASMS

Eight cases of malignant neoplasm were treated with urethane. These included: 4 cases of carcinoma of the stomach with metastasis and 1 case each of melanosarcoma, carcinoma of the rectum, retroperitoneal myxo-

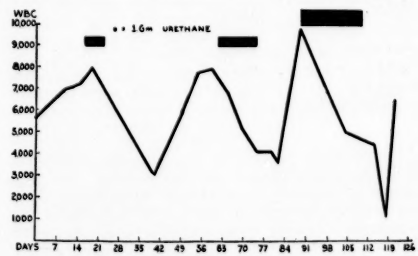

Fig. 6.—Leukocyte-depressing effect of urethane in a nonleukemic patient (with carcinoma of the stomach without clinical change).

sarcoma and lymphoepithelioma of the cervical lymph nodes. There was a twofold reason for using urethane in these neoplastic diseases: (1) to determine whether the disease process could be retarded and (2) to observe

20. Kartagener, M.: Urethan bei Leukämie, Schweiz. med. Wchnschr. **76**: 821-822 (Sept. 7) 1946. Maringer, S.: Urethan-Behandlung der Leukämie, ibid. **77**: 114-115, (Jan. 18) 1947.

the effect of the drug on nonleukemic leukocytes. It is impossible to reach any final conclusion regarding the inhibiting effect of urethane on the course of neoplastic diseases because the number of cases studied is small. All but 2 of the patients were in the terminal stage of the disease and were not ideal subjects for any type of cancer therapy. In the case of lymphoepithelioma the disease had been well controlled with roentgen therapy until recently. The patient enthusiastically stated that she felt much better after the first week of urethane therapy, but this may have been an effect of urethane sedation. It is our impression that in no instance was the course of the malignant disease altered. Others [21] have reported favorable results. Leukopenia developed in 2 cases of carcinoma of the stomach. The leukocytes fell to 1,200 and 2,100. The leukopenia was produced three times in one of these cases (fig. 6). Larger doses of urethane caused a more depressing effect. The leukocyte counts rapidly returned to normal levels after discontinuance of the drug.

EFFECTS ON BLOOD AND BONE MARROW

We have studied the effects of urethane on the morphology of the blood and sternal marrow. Serial marrow aspirations were performed on 6 patients. Little change in morphology of blood or marrow was noticed in acute leukemia. A diminution in the number of primitive cells and a slight tendency toward maturation were occasionally seen. This change appeared to be only temporary. In favorably responding chronic lymphatic leukemia, the absolute number of lymphocytes decreased and smudge cells were less frequently seen. In chronic myelogenous leukemia the blood and marrow showed a great decrease in immature cells. When these patients were in remission with leukocyte levels below 10,000 the blood smears appeared rather normal. Lymphocytes were, however, rarely seen in the smears. Erythropoiesis and thrombopoiesis were not inhibited by urethane in our cases. In 1 of the patients with metastatic carcinoma of the stomach (fig. 6), in whom leukopenia repeatedly developed when urethane was administered, a marrow change developed at these times similar to that seen in the depressed phase of agranulocytosis. The marrow contained a majority of normoblasts. Myelocytes and premyelocytes were infrequently seen and often contained cytoplasmic vacuoles. Similar vacuoles were seen in marrow myelocytes of chronic myelogenous leukemia after urethane therapy (figs. 3 and 4). In 6 nonleukemic patients lymphocytopenia developed while they were taking urethane. In 3 cases this occurred without a significant decrease in the total leukocyte count.

COMMENT

The place for urethane in the treatment of leukemia cannot be designated precisely at this time. The drug appears to be of little or no benefit in producing remissions or prolonging life in acute leukemia. Its action in chronic lymphatic leukemia is variable but, when effective, produces results comparable to roentgen therapy. It is most consistently successful in controlling the clinical and hematologic abnormalities in chronic myelogenous leukemia. The drug has the following advantages: ease of administration and regulation of dosage, a minimum of toxic side actions, a desirable sedative effect and low cost. Jaffe's warning should be kept in mind when prolonged use is contemplated. He found an increased incidence of pulmonary adenomas and malignant hepatomas in rats receiving a prolonged administration of urethane and suggested that this might occur in human beings.[15b] Apparently urethane, like roentgen rays, may at times be carcinogenic.

Urethane may be considered as an additional therapeutic agent available in the treatment of chronic leukemia. We are unable to conclude that it offers any advantage over roentgen therapy other than its ease of administration. We believe that its action is less precise. The drug is more easily administered than are the nitrogen mustards and radioactive phosphorus and, since it is perhaps equally effective in chronic leukemia, its use is to be preferred. Its effects are at times strikingly similar to those of potassium arsenite solution. It is possible that a program of combined therapy consisting of roentgen rays, urethane and nitrogen mustard may be found to be more effective than any one of these therapeutic agents. The nature of the carbamate radical is such that innumerable compounds can be synthesized with it as a component. It is possible that newer compounds which are more therapeutically effective will be found. The mode of action of the carbamates is obscure. Several theories have been suggested but these are based on insufficient experimental evidence. There are indications that the urethanes are nuclear poisons,[22] but whether this is due to interference with purine metabolism,[6] cellular dehydrogenases [23] or other enzyme systems has not been established.

SUMMARY

Urethane (ethyl carbamate) is a potent leukocyte depressant in both normal and leukemic hemopoietic tissues. Satisfactory remissions have been produced in 4 cases of chronic myelogenous leukemia by the oral administration of the drug in doses of 1 Gm. three times a day. Nine patients with chronic lymphatic leukemia have shown a variable response to the drug. Good remissions have occurred in 2 of the patients, some improvement was noticed by 4, and the remaining 3 have died. Severe leukopenia was produced in most of the 9 cases of acute and subacute leukemia without any substantial influence on the course of the disease. No clinical improvement was noticed in 8 cases of malignant neoplastic disease treated with urethane.

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ABSTRACT OF DISCUSSION

DR. CLAUDE E. FORKNER, New York: Leukemia is a disease of unknown cause and without satisfactory treatment. I think we still can say that in spite of this excellent work with ethyl carbamate, or urethane, this new agent does not, in our present knowledge, add much to our ability to treat leukemia effectively. The studies are important, however, because through them new information may be gained which may provide an approach to the understanding of the mechanisms by which the disease may be influenced. The most fundamental facts about the production or destruction of white blood cells are not known. There has been no systematic study of the blood-forming organs with respect to what causes regeneration and destruction of the white blood cells or even of the red blood cells. Our information on these points is only fragmentary. Urethane offers a new tool to add to our armamentarium for the treatment of leukemia. Among the tools which we now have are irradiation by means of roentgen rays, radium, radiophosphorus; the use of arsenic, particularly in the form of potassium arsenite, the use of benzene, which has more or less

21. Footnote 1. Goodman, M. J., and Lewis, H. P.: Urethane in Leukemia, Correspondence, J. A. M. A. **132**: 1105 (Dec. 28) 1946.

22. Dustin, A. P.: Les poisons caryoclasiques, moynes d'analyse cytophysiologique, Arch. d'anat. micro. (spec. no.) **25**: 37-48, 1929.

23. Cadoni, G., and Imperati, L.: Ricerche sulla varia azione dei composti della serie dell'uretano sui processi di deidrogenazione, Riv. di pat. sper. **6**: 65-71, 1930.

been discarded, and the use of nitrogen mustard. All these agents must be used with care. None of them ever cures the disease; all may be dangerous. It is of some importance that the agents which we use to treat leukemia are of themselves carcinogenic. This may be a reason why no known agent is thoroughly satisfactory, because in the treatment of leukemia, we may be simultaneously rendering that person more susceptible to the disorder. The results with urethane correspond somewhat to those achieved with other methods. All these methods are more effective in the treatment of chronic myelogenous leukemia. They are a little less effective in the treatment of chronic lymphogenous leukemia. None of them is effective in the treatment of acute leukemia. Spontaneous remissions do occur, particularly in acute leukemia. Some of the instances in which ethyl carbamate has seemed to be of value may be purely spontaneous remissions. It is too early to judge whether this agent is going to be as effective as other agents, but it seems from our own small experience and from the literature that perhaps it is not as effective as the agents which we now use in the treatment of the disease. The important point to be stressed here is that this new agent may offer an opportunity to learn something about the mechanism of what is going on in the leukemic patient and learn something about the mechanism of blood formation and blood destruction.

DR. LEON O. JACOBSON, Chicago: Working with the nitrogen mustards and more recently with urethane has given some opportunity to compare the therapeutic value of a number of agents. We have used urethane in the following ways: We have attempted to induce repeated remissions in myelogenous and lymphatic leukemia of the chronic variety and in lymphomas, and particularly Hodgkin's disease. After remissions have been induced in the lymphomas and particularly Hodgkin's disease by roentgen ray or nitrogen mustard, an attempt has been made to maintain a long remission by giving urethane. We have also used urethane in metastatic carcinoma of the breast. In our limited experience, we have been able to produce and maintain brief remissions in chronic lymphatic and chronic lymphadenous leukemia, but feel in general that the remissions produced were shorter and less satisfactory from the hematologic and symptomatic point of view than those produced with roentgen therapy, with phosphorus 32, in selective cases, and with nitrogen mustards. In those cases of Hodgkin's disease in which a clinical remission had been produced with roentgen rays or with nitrogen mustards and then urethane was given, we were unable to prolong the remission. These patients had been treated repeatedly for various periods of time with roentgen rays or nitrogen mustard; thus we knew approximately how long remissions could be expected to last in individual cases. Urethane did not prolong the remission or even make it more complete. Cancer of the breast with generalized metastasis was not affected in our limited experience. Urethane seems to control myelogenous leukemia more effectively than lymphatic leukemia. As you know, radiation and nitrogen mustard produce more profound effects on lymphatic tissue than on myelogenous tissue. Further work may indicate that urethane will be useful as an adjunct to roentgen rays in various neoplasms. The results obtained thus far by various workers using urethane, nitrogen mustards and other chemotherapeutic substances have given a definite stimulation to work on the modification of these compounds and the search for other more effective chemotherapeutic agents. Even with these agents the treatment of these diseases is unsatisfactory at present. I would like to ask Dr. Hirschboeck to tell a little more of the toxicity which he encountered in his cases.

DR. EDWIN E. OSGOOD, Portland, Ore.: As a part of a long term study of the fundamental nature of growth at the University of Oregon Medical School along the lines that Dr. Forkner mentioned, Dr. Chu I-Tung and I have included a study in marrow cultures of the action of urethane. I should like to ask Dr. Hirschboeck whether he has noted changes in the granulocyte series similar to those that I will show. In the marrow culture, we have a method for controlled quantitative study of living human cells. We were able to compare the action of 200 kilovolt roentgen rays, radioactive phosphorus, neutron rays, million volt roentgen rays, colchicine, urethane and nitrogen mustards. I want to show the changes that occurred in the cells in the urethane series which were not observed in the controls or with any of these other agents. The first thing noticed was an increase in the number of mitoses occurring as early as three hours and reaching a maximum at twenty-four hours. This doubtless accounts for the increase in cell count observed early by Dr. Hirschboeck. The most common change noted and seen chiefly in granulocytes and progranulocytes was that the basichromatin is aggregated in clumps with persistence of the nuclear membrane. A less frequently observed effect was complete loss of nuclear membrane with fragmentation and karyorrhexis rather than a colchicine-like effect. The number of fragments were too few for them to be altered chromosomes, and they were more rounded than with colchicine. Urethane does not affect all the cells. A common development after the third day was the appearance of double nuclei in cells of the granulocyte series, first in the progranulocyte and later in more mature cells. Such double nucleated cells are extremely rare in the granulocyte series, though common in cells that divide by amitotic division. Clinically, we have observed similar results to those reported by Dr. Hirschboeck but agree with Drs. Forkner and Jacobson. We feel that results from urethane are inferior to those with regularly spaced total body irradiation or injections of radioactive phosphorus. In the 1 case of malignant tumor reported in the correspondence section of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION by Goodman and Lewis we observed the most striking regression in a metastatic malignant tumor that I have ever seen with any method of therapy.

DR. WILLIAM DAMESHEK, Boston: I had the occasion yesterday in the Section on Experimental Medicine and Therapeutics to discuss two other chemotherapeutic methods, namely, the use of nitrogen mustard in Hodgkin's disease and the use of "stilbamidine" in multiple myeloma. It is possible that we may now be at the threshold of a chemotherapeutic era for the treatment of the proliferative disorders of the white blood cells. Urethane has a definite effect, particularly in chronic myelogenous leukemia. In relatively early cases an excellent remission may be obtained, and this can be continued for at least a few months by the use of the drug in relatively small dosage. In the severe cases with a large spleen, some effect on the white cell count may be obtained, but there may be little reduction in the size of the spleen. In these and other cases of advanced chronic myelogenous leukemia, roentgen therapy appears to be far more effective than urethane. What is more, when the drug is discontinued or its dosage diminished, there is usually a quick relapse, with a rapid rise in the leukocyte count to high levels. One great advantage of the various chemotherapeutic methods which are now in the process of development is that they allow complete control of therapy by the internist or hematologist rather than the divided control which is essential in roentgen therapy. The radiologist naturally likes to control his own particular apparatus, and we like to control our patient. Often some degree of conflict occurs, which will be avoided as chemotherapeutic methods continue in their development. It is the hope for the future that continued study in this field will lead to methods for the control of the abnormal metabolic activities of the proliferating white cells.

DR. JOHN S. HIRSCHBOECK, Milwaukee: In answer to Dr. Jacobson's question regarding toxicity, I may state that we believe that urethane may cause two types of nausea and vomiting. One is due to a local gastric irritation occurring in a few patients after the ingestion of as little as one or two doses of the drug. The other appears to be central in origin and occurs late in the course of therapy, even when enteric-coated capsules are used, and may persist for several days after the drug is discontinued. One of the patients with chronic lymphatic leukemia showed evidence of nephritis at autopsy. This may have been a toxic effect of urethane. We have not noticed morphologic change in the blood or marrow other than the cytoplasmic vacuoles which were described. Urethane therapy is, of course, still experimental. We feel that the drug is of definite value in chronic myelogenous leukemia and should be used to supplement or substitute for roentgen therapy. It is particularly suitable for patients who do not live near a roentgen therapy center.

Special Article

CANCER OF THE NERVOUS SYSTEM

Brain, Spinal Cord and Peripheral Nerves

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and
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San Francisco

This article is the fifth of a series to be published by the American Medical Association in cooperation with the American Cancer Society. The series is designed to aid in the early diagnosis of cancer and thereby to gain more effective results in treatment. When complete, the series will be published in book form by the W. B. Saunders Company under the sponsorship of the American Medical Association and the American Cancer Society.

Since the end of World War I impressive advances have been made in our knowledge of the biologic characteristics, modes of early diagnosis, and treatment of tumors affecting the nervous system. It is now recognized that these tumors, once considered rare, constitute 2 per cent of all cancers. The early diagnosis of this group has been materially aided by improvement in the knowledge of the physiology of the nervous system as well as by technical developments, notably pneumoencephalography, cerebral angiography, myelography and to some extent electroencephalography.

Through improvement of surgical and anesthetic technic the operative mortality in brain tumors is at a level comparable with that of major surgical operations elsewhere in the body. The percentage of surgically curable tumors is gradually being enlarged. Improvement in roentgen therapy is prolonging the useful life of increasing numbers of patients with nonremovable growths.

The side effects of brain tumors have also become controlled more satisfactorily during this period of time. Convulsions, which are one of the most frequent complications of brain tumors, are reduced in frequency or are eliminated entirely by a variety of anticonvulsant drugs which have been developed in recent years. Improved knowledge of endocrine function has minimized the distressing effects of tumors of the intracranial endocrine glands and centers. Developments in these two particular lines have reduced the incidence of psychic disturbance resulting from the projection of endocrine or convulsive disease into the patient's life.

INTRACRANIAL TUMORS

The term intracranial tumor has come to include all the intrinsic tumors of the brain, the pituitary and the pineal glands, the cranial nerves and the meninges as well as those tumors of the skull which come to invade the intracranial space. Daughter growths from cancer elsewhere in the body also are included.

Successful treatment of an intracranial tumor depends on its type, its accessibility, the extent of its involvement of important areas (speech, motor, medulla) and the stage at which it is diagnosed. More than 50 per cent of all brain tumors fall in the favorable group if there is reasonably early diagnosis and if the treatment is properly executed.

From the Department of Neurosurgery, University of California Medical School.

EARLY DIAGNOSIS OF TUMOR OF THE BRAIN

Tumor must be thought of whenever the symptoms and signs are those of a progressive single lesion. The onset usually is insidious but occasionally is precipitous as in glioblastoma multiforme. Certain generalities may give some support to the early suspicion that a neoplasm may be present. Thus, most tumors in adults occur above the tentorium; a notable exception is the cerebello-pontine angle tumor, or perineurial fibroblastoma of the eighth (auditory and vestibular) nerve. As with all other growths, brain tumors in adults have their highest incidence in the cancer age of the fourth, fifth and sixth decades. Most brain tumors of childhood are of the cerebellum, with the supratentorial exception of the epithelial cysts near the pituitary (Rathke's pouch cysts, craniopharyngioma). These general trends, however, are valuable only as positive support for an impression of tumor and not in a negative way to rule out other etiologic factors.

Brain tumor may manifest itself in three ways: first, by local irritation of some structure of the central nervous system which produces a convulsion or some other evidence of uncontrolled nervous discharge; second, by focal paralysis of some part of the brain, or of one or more cranial nerves, which diminishes or eliminates thereby the function of the part affected; third, by an increase of intracranial pressure because of the size and space-occupying nature of the tumor, or because its presence blocks the pathways of cerebrospinal fluid between the ventricles and the site of absorption. Signs of local irritation or of local pressure usually are earlier signs than are those of general pressure, though some tumors by their location may block the fluid pathways at a relatively early date.

Convulsions which start in adult life constitute one of the more frequent early signs of tumor affecting the cerebrum. The neurologic axiom has developed that the initial appearance of convulsions in an adult must be regarded as evidence of a brain tumor until proved otherwise. Both intrinsic and extrinsic tumors may irritate the cortex, thus producing such a discharge. In the so-called silent areas of the brain the tumor may reach considerable size before manifesting itself in this way, but in the more responsive regions tiny growths may thus give evidence of their presence. If the motor cortex is affected a jacksonian type of fit may be anticipated. If the somatosensory cortex is involved a sensory pattern of numbness, tingling, electricity or pins and needles in the affected part may predominate in the early phases. If the inner aspect of the tip of the temporal lobe is involved olfactory or gustatory hallucinations may be observed. Tumors around the sella turcica may produce these phenomena. If the upper posterior part of the temporal lobe is affected there may be auditory hallucinations. Visual hallucinations come from irritation in the occipital region. The appearance in an adult of hallucinatory phenomena, recurrent and of a fairly regular pattern, should make one think of an early brain tumor. If the lesion involves the dominant hemisphere, transitory difficulty in speech may be an early manifestation of brain tumor and should be regarded as an irritative phenomenon, probably originating in the depths of the hemisphere.

Focal paralysis of function may appear after an initial period of irritation or may occur as an initial symptom. Weakness of an extremity progressing both as to degree and as to extent of involvement may occur if a tumor is developing in the motor cortex. The progress of a

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weakness from one extremity to its fellow on the same side, such as from the right leg to the right arm, should be particularly suggestive. Reflexes are usually increased and pathologic reflexes may be present. Involvement of the postcentral cortex may result in progressive loss on the opposite side of stereognosis, recognition of figure writing on the skin and identification of texture, form and weight (deep sensation). Defects in the visual fields may result from a lesion involving the optic tract anywhere between the occipital lobe and the optic foramen; a lesion posterior to the optic chiasm would produce a defect homonomous in character; one anterior to the chiasm would probably affect one eye alone. Focal lesions below the tentorium may paralyze single or successive groups of cranial nerves. Involvement of the cerebellar tracts or nuclei will produce impaired coordination.

Alteration in temperament may be an early manifestation of a brain tumor, particularly of the intrinsic type (glioma). This seldom persists for any long period of time as an isolated complaint. Most temperamental changes are associated with either frontal or temporal lobar lesions. Some personality change may appear in conjunction with generalized increase in intracranial pressure. Overt psychopathic states are not common.

The usual symptoms of increased intracranial pressure are of generalized headache, drowsiness, nausea, vomiting and slowness of the pulse. Ocular papilledema (choked disks) almost always occurs. In the child a cracked-pot note may be elicited on tapping the skull. If the pressure is the result of a tumor in the region of the third ventricle there may be associated metabolic changes such as increase in weight, altered sexual activity and changes in water metabolism. A block at the aqueduct of Sylvius may add interference with conjugate movement of the eyes in an upward direction. A block in the region of the fourth ventricle may produce ataxia, nystagmus and weakness or paralysis of cranial nerves.

Once a growth is suspected special studies may be necessary to positively identify the tumor. Plain roentgen ray films of the skull may show localized erosion, proliferation of bone or unusual vascular markings. Tumors of or near the pituitary may enlarge or deform the sella turcica. Decalcification of the dorsum sellae is characteristic of generalized intracranial pressure. Tumors arising from the eighth nerve sometimes enlarge the internal auditory canal. Deposition of radiopaque material such as calcium may appear in almost any type of neoplasm; occasionally it is seen in certain of the cysts, such as Rathke's pouch cyst; it may also occasionally be seen in the walls of aneurysms. Probably the most valuable lateralizing sign of tumor to be obtained from roentgenograms of the skull is that of shift of a calcified pineal gland away from the side of a tumor. Occasionally in lateral films its displacement in the anterior-posterior direction may be demonstrated. Deposits of calcium in the choroid plexus must not be mistaken for a displaced pineal gland.

Roentgen studies following replacement of the ventricular and subarachnoid fluid with air or oxygen may give further valuable information. If the pressure of the spinal fluid is normal, this procedure can be performed by the lumbar route (pneumoencephalography); if the pressure is elevated, bur openings are made in the skull and the air is introduced directly into the ventricular system (ventriculography). By this method it is often possible to localize the tumor accurately, and at times its possible nature may be suggested. This procedure should be carried out only when equipment and personnel will permit it to be followed immediately by operative treatment should this be found necessary.

The recent development of carotid arteriography, wherein radiopaque material is injected into the carotid arteries while roentgenograms are taken in rapid series, has opened up still further fields of study. Arteriograms are particularly adapted to early demonstration of tumor and may occasionally be of some value in the identification of the type of tumor.

GLIOMAS

Gliomas, which are the intrinsic tumors of the brain, constitute approximately 50 per cent of all intracranial tumors. These growths are composed of neurectodermal cells, most of which are glial in character, though tumors containing neuronal elements are included. In a general way the cells of tumors of this group are similar to glial cells in various stages of embryonic growth and development, and the nomenclature now generally accepted, based in large part on that developed by Bailey and Cushing in 1926, reflects this apparent relationship between embryonic and neoplastic cells.

All gliomas, being invasive growths which tend to recur locally, must be regarded as malignant tumors. Recurrence can be eliminated or significantly delayed only through early recognition and treatment before essential areas have become invaded by the neoplastic process. When the tumor arises in such a region, the problem, of course, is resolved as it commences.

Astrocytoma.—The astrocytomas, which constitute somewhat more than one fourth of the gliomas of the brain, are the commonest of the gliomas. About 65 per cent of the astrocytomas are cerebral, approximately 18 per cent arise in the cerebellum and approximately 10 per cent occur in the brain stem and the region of the third ventricle. The sex incidence of astrocytoma is about evenly divided. The age incidence in the cerebrum and in the cerebellar hemispheres is greatest in the fourth and fifth decades. In the cerebellar vermis the incidence is highest in the first and second decades. The period of symptomatologic manifestations and the survival depend not only on the type of tumor growth but on the location.

There are three subtypes of astrocytoma. Fibrous (piloid) astrocytomas are composed of cells rich in fibers, with small nuclei scattered throughout the neoplastic mass. These tumors are found in the cerebrum and in the cerebellum. The cerebral groups are firm, pale and gelatinous and may contain small cysts or occasionally a large one. By involvement of whole gyri and by their firmness they may give a false appearance of being well demarcated. In the cerebellum large cysts containing yellow fluid which clots on removal are frequently encountered. In these the active tumor usually is found as a nodule in some portion of the cyst wall (mural nodule), removal of which is often completely curative. Of all the gliomas this tumor carries the best prognosis. Survivals of over three years following extirpation of cerebral astrocytomas are not at all uncommon.

Protoplasmic astrocytoma (diffuse) is more commonly seen in the cerebrum. The cells infiltrate the white and gray matter, stimulating satellitosis about nerve cells and stifling their activity by force of numbers of invading cells. These diffuse tumors may cause irritation and produce convulsions, but they progress so insidiously that a mass may not be evident until late in the disease. At operation a generalized widening of

gyri and narrowing of sulci may be seen, but the limits of the tumor may be poorly defined. The tumor type can be identified by biopsy. Fortunately this tumor is fairly responsive to roentgen therapy.

Gemistocytic astrocytoma, composed predominantly of Nissl's plump cells, is the third variant of the astrocytoma group. This tumor also is more commonly found in the cerebrum. It is the most rapidly growing of the astrocytomas, has the shortest history and is the most unfavorable of the group. Its preoperative history is usually but slightly longer than that for glioblastoma multiforme; postoperative survival, however, is significantly longer. Grossly these tumors are usually reddish and gelatinous or meaty in appearance. Cysts are uncommon and when present are usually small, probably representing areas of degeneration. The invasive proclivity of the tumor is midway between that of the protoplasmic astrocytoma and the suggestive encapsulation of the fibrous astrocytoma. The tumor is not as solid as the noncystic fibrous astrocytoma. Areas of degeneration may cause it to be mistaken for glioblastoma multiforme, grossly as well as microscopically. Postoperative survival of from one to two years is not uncommon. As with other tumors predominantly cerebral in location, the problem of convulsions may be a major one.

Glioblastoma Multiforme.—The second most common of the gliomas, constituting about one fourth of this group, is glioblastoma multiforme (spongioblastoma multiforme). It occurs far more frequently in the cerebrum than elsewhere, although it has been described in the brain stem and the cerebellum as well as in the spinal cord. It affects males more frequently than females in a proportion of about three to two. The age incidence is greatest in the fourth, fifth and sixth decades; however, instances have been described in the very young and the very old. Glioblastoma multiforme may come on with precipitous suddenness, striking a man in the prime of life completely without warning. The sudden onset may be so striking as to cause confusion and an erroneous diagnosis of a vascular accident. The progress of the disease, however, will usually give early evidence that the problem is no ordinary hemorrhage or thrombosis. The average total duration of symptoms is between six months and a year. However, patients who have been treated early and radically have survived as long as five years after the first diagnosis. About one third may be expected to live longer than one year if removal is accomplished early and is combined with roentgen therapy.

Glioblastoma multiforme appears to originate most commonly in the white matter of the brain and tends to travel by the tracts of the brain, crossing to the contralateral side by the corpus callosum and going into the brain stem by way of the major pathways to and from the cerebrum. It invades the gray matter indiscriminately, however. The tumor is usually soft and succulent, containing large areas of degeneration. Cysts of varying size, which contain reddish yellow fluid, may be encountered. These may develop in a relatively short period of time. Large vascular channels, some of whose walls apparently take part in the neoplastic process, course through these growths. Occasionally firm tissue of mesoblastic origin may be found at the surface. The tumor may have the appearance of being encapsulated, but deeper it will be found in continuity with the underlying white matter. Variations in color and occasional small collections of frank clots suggest that extravasations of blood may occur in these tumors with some degree of frequency.

Microscopic study reveals cells of varying size and type. There is no recognized cell which is named the glioblast. The cells of the tumor include almost every variant of the glial series. The blood vessels show striking proliferation of the adventitia and intima, suggesting that the vascular system plays a role in this neoplastic process greater than that usually found in other tumors of the glioma series. Frank obliteration of vascular channels with recanalization and vascular budding also is observed.

If glioblastoma multiforme is encountered early and in an area from which it can be extensively removed, many months of useful and pleasurable life may be anticipated for the properly handled patient. Those tumors originating in more vital centers are, of course, difficult to handle and carry a proportionately increasing gravity of outlook with the importance of the center affected.

Medulloblastoma.—Medulloblastoma is the commonest glioma of childhood. It constitutes about 14 per cent of all the gliomas. This tumor practically always arises in the cerebellum and involves the fourth ventricle at an early stage. Males are affected more than females in the proportion of two to one. The average age is in the latter half of the first decade, but the tumor is fairly commonly seen throughout the first decade and into the first half of the second. Because this tumor occurs so frequently during a period when a certain degree of clumsiness is anticipated, the early signs of incoordination are not apparent or are ignored until signs of generalized pressure appear. A story of recurrent bouts of headache, nausea and vomiting culminating in recognition of impaired coordination or reduced vision due to extensive papilledema is all too common. Children with recurrent attacks of nausea, vomiting and headaches should be observed for changes in coordination, for changes in the note on tapping the skull and for evidences of papilledema.

Medulloblastoma is usually a soft, friable, cyanotic mass with little supporting connective tissue, and when presenting into the ventricle is covered at the surface by a filmy membrane no thicker than the arachnoid. Its friability permits cells to float out into the subarachnoid space, setting up daughter growths in the spaces of the cranium and of the spinal canal. The appearance of encapsulation is a false one, for the tumor is quite invasive. Because of its location and proximity to the brain stem it can never be regarded as having been completely removed surgically. Fortunately, it is responsive to roentgen therapy, which should always be used in addition to surgical procedures. Survivals of from one to five years are not at all uncommon in medulloblastoma when roentgen therapy is judiciously used in conjunction with treatment by surgical means.

Cerebellar Sarcoma.—A tumor in the cerebellum of older persons, having cells morphologically similar to those seen in medulloblastoma of childhood but associated with more extensive reticulin formation, the cerebellar sarcoma has been the subject of considerable discussion among neuropathologists. Some regard this tumor as essentially the same as the medulloblastoma of childhood. Others have regarded it as a cerebellar sarcoma differing from cerebellar medulloblastoma in all characteristics except its usual anatomic location.

Ependymoma.—Ependymoma constitutes about 10 per cent of the gliomas. This tumor is widely distributed

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through the cerebrum, brain stem and the spinal canal, being the most frequently observed glioma of the spinal canal. It is reported more frequently in females than in males in a proportion of about two to one. The age incidence of the tumor in the brain reaches a peak in the third and fourth decades. In the cerebellum and brain stem it has a tendency to rise from the floor of the fourth ventricle and has been described in this location in the first few years of life. It is a fairly common glioma of childhood in the cerebrum.

Cerebral ependymomas frequently have connection with the ventricular system; a large percentage of the gliomas going into the lateral ventricles are ependymomatous in character. They are usually moderately firm, but cysts may be encountered. They grow slowly, the symptoms persisting for up to three or four years before their nature is manifest. Ependymomas of the posterior fossa usually block the fourth ventricle early in their course, giving rise to generalized increased pressure as an early sign. The postoperative survival in ependymomas depends on the location. Survivals up to five years are not uncommon. The tumor is fairly resistant to the therapeutic effect of the roentgen ray.

Polar Spongioblastoma. — Polar spongioblastoma (spongioblastoma polare) is most commonly seen in the region of the pons, the optic chiasm and the corpus callosum. The course of the disease is usually slow and insidious. The symptomatology is that of progressive involvement of the area of origin; that is, progressive loss of vision in tumors of the chiasm, progressive involvement of successive cranial nerves at their nuclei of origin if the pons is affected. The tumor cells insinuate themselves into the tracts or nuclei, finally stifling function by their overgrowth. Generalized pressure occurs late with tumors in the chiasm and is almost unheard of with those in the pons. These tumors in the corpus callosum are characterized by the mental disturbance so commonly seen in primary lesions of the corpus callosum. Disorientation, fabrication and delusion are frequent manifestations of such lesions.

Polar spongioblastoma constitutes about 5 per cent of the gliomas. It is slightly more common in the male than in the female. The age incidence of the tumor in the pons and in the chiasm is through the latter part of the first and into the second decade. Polar spongioblastoma of the cerebrum elsewhere, and particularly of the corpus callosum, is a tumor of adult life with a peak in the fourth and fifth decades.

This tumor is usually not amenable to surgical intervention because of the regions which it commonly involves. It is moderately susceptible to roentgen therapy, particularly in the basilar region. Patients have been carried along successfully for several years by the judicious therapeutic use of roentgen rays.

Oligodendroglioma.—About 5 per cent of the gliomas are oligodendrogliomas. The tumor may be indolent, and symptoms, in which convulsions predominate, may continue over several years before the identity of this slowly developing growth becomes manifest. Nearly all oligodendrogliomas are found in the cerebrum. They appear to commence in the white matter and slowly invade the adjacent gray. The age incidence is greatest in the fourth and fifth decades. The tumor appears to affect male and female about equally. Because of its slowness of growth, calcification is commonly found in the tumor. The tissue is usually moderately firm, but its area of extent is poorly outlined. Cysts are rare.

Periods of survival up to several years following surgical intervention are frequently seen. This is regarded as being related to the slowness of growth inherent in this tumor rather than to the successful extirpation of the entire lesion. Sudden changes in the rate of growth are particularly common in this tumor, and changes in cell types may be found at subsequent examinations. The tumor is but moderately responsive to the effect of the roentgen ray.

MENINGIOMAS

Tumors of the meninges constitute approximately 16 per cent of brain tumors. They are most frequently encountered above the tentorium and therefore affect the cerebrum more frequently than the cerebellum and brain stem. They are found in females more frequently than in males in the proportion of about three to two. The age incidence is highest in the fifth decade, one third of Cushing's series, for example, being first observed in this period. Instances have been reported, however, from the first to the ninth decades of life. Interestingly, the average age of symptomatic onset is apparently about eight years younger than that for initial study, and patients are reported to have had convulsions for thirty years before treatment of a causative meningioma. Most of these tumors, however, will not permit such a lag between onset and treatment. The average rate of progress is fairly rapid, being a matter of only months in some cases.

Because of the location of the majority of meningiomas in relation to the cerebrum, convulsions are a major initial symptom. Sometimes the tumor will invade the skull, producing a bump on its outer surface which indicates its presence; sometimes progressive paralysis will occur without preceding irritative phenomena. Meningiomas at the base may block the cerebrospinal fluid pathways and produce generalized pressure as an initial symptom.

Meningiomas usually arise from the arachnoid, though there is generally an attachment to the dura and some primary tumors of the dura have been described. The tumor may grow primarily into the cranial cavity and may not produce demonstrable change in the adjacent bone. It may produce a thickening of the inner table of the adjacent skull; cells may invade the haversian canals to produce thickening of the inner and outer tables; invasion of the skull may reach the point at which there will be an erosion with considerable projection of tumor into the subgaleal space on the outer surface of the skull. The growth of most meningiomas is associated with a striking increase in vascular supply, and at times this will be manifest in plain roentgen ray films of the skull.

It is generally considered that there may be some relationship between these tumors and the arachnoidal granulations. The usual location of these tumors, which is most frequently close to one of the major dural sinuses, has some bearing on this possibility. Tumors of the olfactory groove and the tuberculum sellae are not uncommon.

Usually these tumors push the brain ahead of them and do not invade it. There may be pressure erosion of the pia, however, and extremely nodular tumors may come to incorporate isolated bits of brain in the crevices between the projecting nodules, producing, from a practical standpoint, invasion of the cerebrum itself.

The prognosis in meningioma is in general better than that for tumors of the glioma group. The striking vascularity plus the tendency to invade the dural sinuses, which are so frequently adjacent, may make the removal a complicated one, sometimes requiring more than one

operation. Tumors attached to the sagittal sinus or the torcular, or plaque tumors overlying these essential structures, may recur, but the tumor type seldom changes and reoperation is to be regarded as justifiable when necessary. Meningiomas have been regarded as resistant to roentgen therapy, though favorable results are beginning to appear in the recent literature. The major complicating factor in meningioma is the convulsive state which may result from irreversible changes in the adjacent brain. These are controlled by the usual anticonvulsive regimen.

CEREBELLO-PONTINE ANGLE TUMOR

Cerebello-pontine angle tumor (eighth nerve tumor; neurinoma of the eighth nerve; perineurial fibroblastoma of the eighth nerve; acoustic neuroma) is said to constitute about 10 per cent of intracranial neoplasms. This tumor usually arises from the perineurium of the acoustic nerve just at or in the porus acousticus. It affects females more than males in the proportion of three to two and is most commonly found in the fourth and fifth decades of life. These growths may be bilateral, and their occasional association with von Recklinghausen's disease (neurofibromatosis) has been reported. The usual early symptoms are progressive loss of hearing in one ear, sometimes with tinnitus and occasionally but not commonly with some dizziness. Attacks of dizziness, such as those seen in Ménière's syndrome, are rare. Because of the proximity of the facial nerve in the porus acousticus, some involvement by pressure, manifesting itself as weakness of movement of the face, may be seen, usually as a late manifestation of the disease. As the tumor enlarges it may press on the ninth, tenth and eleventh nerves as well as the fifth and the third anteriorly. It may grow in front of the pons and may so distort the brain stem as to produce some signs of involvement of the opposite side, even when bilateral tumors are not present. It may press on the tract and the nuclei of the cerebellum to produce signs of cerebellar disease, again as a late manifestation of the tumor.

The tumor is usually encapsulated. Inside the capsule there may be areas of cystic degeneration, occasionally of gratifying size. Much of the tumor ordinarily is yellow and soft, but the presence of firm, fibrous trabeculae with ample blood vessels is common and makes removal difficult. It usually has a network of blood vessels over its capsule, and there may be intimate adhesions between it and the brain stem, the medulla and pons. The seventh nerve is commonly bound up in the wall of the tumor so that complete extirpation, at least in the late stages, is usually associated with paralysis of the seventh nerve.

When located early, these tumors can be completely removed and the patient cured with no incapacity other than the loss of hearing due to sacrifice of the affected eighth nerve. Unfortunately, they are seldom discovered before there has been involvement of other cranial nerves and of the brain stem to the extent that complete removal is difficult or impossible. In such circumstances the surgeon generally has resort to subtotal intracapsular removal. Since the tumor does not ordinarily change its cytologic characteristics, reoperation when the tumor recurs is justifiable and patients may be carried along for many years of happy and useful life. The tumor is but moderately responsive to roentgen therapy.

Nowhere in brain tumor surgery is the necessity of early diagnosis more striking than in the case of this tumor. Most patients with it have had a history of progressive loss of hearing on one side for many years. If one waits for evidence of involvement of the cerebellum or of other cranial nerves, the tumor is already too large to be approached without great hazard and the chance of getting a complete extirpation is materially reduced. Erosion of the porus acousticus, when definite, is a good positive sign; but its absence is a poor negative one, for the site of origin of many tumors is such that involvement of the bone occurs late or not at all. Nerve type loss of hearing that is unilateral and progressive should be regarded as potentially due to a tumor of the eighth nerve until proved otherwise.

Tumors similar in pathologic characteristics to that arising from the eighth nerve have been found arising from other cranial nerves, notably the tenth. Under such circumstances the symptom complex is that of progressive involvement of the nerve affected, those adjacent and, of course, the brain stem and cerebellum.

PITUITARY TUMORS

The incidence of adenomas of the pituitary gland is reported in widely varying figures, presumably related to the particular interests of the investigator. Probably the incidence is about 5 per cent of all intracranial tumors. Primary tumors of the pituitary are most commonly adenomas of the anterior lobe. Of these, chromophobe adenomas are two and one-half to three and one-half times more common than the next most frequent type, the eosinophilic adenoma.

Chromophobe adenomas give evidence of their presence by progressive reduction of sexual activity and other endocrine function. Pressure on the optic chiasm producing impairment of vision, usually having some or all of the aspects of bitemporal hemianopsia, may be the first sign. Some tumors may burst laterally from the sella turcica, compressing the third, fourth, fifth or sixth cranial nerves or irritating the hippocampal gyrus, thus producing uncinate fits. The tumor may grow into the posterior fossa, producing pressure on the brain stem as a late manifestation.

Eosinophilic adenomas are responsible for the well known syndrome of acromegaly quite early in their development. They usually do not reach the size that is common with the chromophobe adenomas but may produce similar changes in the visual field.

Basophilic adenomas are not regarded as reaching such a size as to make them of surgical importance.

Usually the surgical treatment of pituitary adenoma (chromophobe and eosinophilic) is directed toward the preservation of vision, and it is most effective early when the defect is confined to the bitemporal fields. Delay seriously increases the probability of permanent visual impairment. In advanced stages the mere decompression of the nerve by removal of the tumor may alter the physiologic relationship and result in complete blindness. Delay to such a point, however, is indefensible, since the clinical history plus roentgenograms of the skull showing enlargement of the sella turcica are seldom atypical. In the rare instance in which sellar enlargement is not demonstrable, progressive visual loss demands the use of encephalography for study of the parasellar region.

Pituitary adenomas are sometimes cystic. It may be feasible to remove an early growth completely, sometimes preserving a considerable amount of normal pituitary gland. The tumor cells are moderately sensitive to roentgen radiation. The initial swelling which follows roentgen radiation may cause increasing loss of

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vision, however, and it is usually considered advisable to decompress the optic nerve surgically first. Another reason for advising surgical decompression first is that other tumors insensitive to roentgen radiation may mimic the effect of pituitary adenoma.

TUMORS OF THE HYPOPHYSIAL DUCT

Tumors arising from cell rests brought into the region of the sella turcica by the forerunner of the anterior lobe may give rise to epithelial tumors in or above the sella turcica (Rathke's pouch cyst; craniopharyngioma; pituitary adamantinoma). Slowly growing and usually cystic, they give evidence of their presence by pressure on the pituitary gland. They produce delayed sexual development or alteration of sexual function if puberty has already been reached. They may press on the structures in the region of the third ventricle, producing metabolic changes, dwarfism and obesity; by pressure on the optic nerve they impair vision. Unlike the pituitary adenomas, these tumors are usually seen in the first, second and third decades of life. Roentgenograms of the skull will commonly show changes in the sella turcica. There may be calcification in the walls of the cyst permitting it to be identified on this basis alone. These cystic tumors are not susceptible to roentgen therapy, but surgical extirpation, while often incomplete because of attachment of the tumor to vital centers, may be expected to give dramatic symptomatic relief, particularly with respect to vision. Early diagnosis and close medical supervision usually permit a favorable outlook for many years. Failure of sexual maturation presents a more difficult problem of therapy; by the time the diagnosis is made irreversible changes often have occurred.

EPIDERMOID AND DERMOID CYSTS (CHOLESTEATOMA; PEARLY TUMOR)

Wherever in embryonic life there has been infolding of the ectoderm, the inclusion of epithelial cells which maintain their more primitive characteristics of epithelium is possible, and the proliferation of these cells produces cystic tumors. If only the ectoderm is involved the resulting cyst is an epidermoid; dermoid cysts contain ectodermal and mesodermal elements. The rare teratoma will contain elements of all three germ layers.

In the cranium epidermoid and dermoid cysts are found in the third ventricle, in the posterior fossa and in the skull itself at points where there is infolding, as at the lateral margin of the orbit. The tumors give evidence of their presence by pressure on adjacent structures. In the third ventricle increased intracranial pressure is a common early sign. The tumors appear in the first three decades of life most commonly, though their slow growth may delay evidence of their presence until as late as the seventh decade. These cysts are encapsulated and when not intimately adherent to adjacent vital structures may be completely removed. If not totally removable, excavation of the content of the cyst may ameliorate symptoms for prolonged periods of time.

VASCULAR TUMORS

Angiomas.—Angiomas may affect the brain at any age and may manifest themselves at any age level, but generally evidence is present in the first three or four decades of life. Angiomas are generally regarded as congenital malformations of blood vessels, which enlarge by expansion of the vessels already present rather than by direct proliferation of cells. Three types of tumors are recognized; namely, telangiectases, and venous and arteriovenous angiomas. They usually manifest themselves by the production of convulsions, probably due to scarring which results from the enlargement of the vessels and occasional small hemorrhages. Calcium is often laid down in the wall of these vessels, and the tumor then may be identified by plain x-ray films. The arteriovenous angiomas may have an accompanying bruit, giving a clue to the nature of the disease. Port-wine nevus in the distribution of the fifth cranial nerve may be associated with hemangioma of the brain. A patient with a port-wine nevus of the face who has convulsions must be considered as probably having an angioma of the brain.

Telangiectatic hemangiomas occasionally are removable lesions. The bulk of angiomas are cavernous in nature, however, and are not amenable to surgical or roentgen therapy. Unequivocal localization and diagnosis of this group are often possible through the arteriogram. Since these tumors do not grow, the chief problem is that of control of the convulsions which so frequently are the only cause for complaint.

Hemangioblastoma.—The hemangioblastoma, a tumor of proliferating embryonic blood vessels, may occur in middle life. It usually is found in the posterior fossa, giving evidence there of a slowly progressive, expanding lesion. This tumor is often cystic, the neoplastic part being preserved as a mural nodule. It is susceptible to roentgen therapy to a moderate degree. There may be an associated angioma of the retina and cystic degeneration of the parenchymatous organs of the abdomen (Lindau's disease).

INTRACRANIAL GRANULOMA

Granulomas in the brain may produce symptoms indistinguishable from those of neoplastic growths. Tuberculoma is the one most commonly encountered nowadays. It may be calcified and in certain regions may be successfully excised. Though occasional gummas are still to be seen, meningovascular syphilis is a more frequent mimic of an intracranial tumor. The diagnosis is made by serologic studies, and treatment is antisyphilitic.

Since the Leyte campaign, several instances of granuloma from schistosomiasis japonica have been reported, the granuloma behaving in all clinical respects like an expanding neoplasm of the cerebrum. Excision coupled with appropriate systemic treatment has generally been satisfactory in control of the disease.

METASTATIC TUMORS

Malignant disease elsewhere in the body may metastasize to the brain. Sometimes the intracranial metastasis will be the first evidence of the mother tumor. Cancers in the thoracic cage, of retroperitoneal origin, and of the breast, and malignant melanoma are common sources of intracranial metastases. Cancers in the throat and neck may invade the cranium by direct extension and erosion.

When circumstances indicate a single cerebral metastasis and the mother tumor apparently is under control, extirpation of the cerebral metastasis may be justified. Metastatic tumors in the brain are usually surrounded by an area of necrotic cerebral tissue and often may be completely eradicated. They ordinarily produce little general reaction on the part of the brain, and the patient may recuperate with surprising rapidity. The uncomplicated survival for many months following extirpation of a single cerebral metastasis is most gratifying for all concerned.

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NEOPLASMS OF THE SPINAL CORD

When a patient complains of a progressive alteration in sensation or in motor power in the lower extremities, or in all four extremities; when there is progressive impairment of bladder function and, in the male, progressive sexual impotence; when there is a constant and progressive radicular pain, usually worse at night, one must think of a possible tumor of the spinal canal involving the spinal cord either primarily or by pressure from without. This series of complaints demands complete investigation by thorough neurologic examination, roentgenologic study of the suspected region, spinal puncture with the Queckenstedt (jugular compression) test, chemical study of the spinal fluid and myelography with one of the radiopaque oils. Tumors high in the spinal canal may produce scoliosis as an early manifestation of their presence, particularly when they occur before the fourth decade.

Fifty per cent of tumors affecting the spinal cord are completely removable, and if removal is accomplished before irreparable damage to the cord has been done, a good result may be anticipated. If the presence of tumor is not recognized and anatomic changes of an irreversible character are produced by it, the result must be most distressing, no matter what the type of lesion. Therefore it is readily recognized that early diagnosis in the case of tumor of the spinal cord is imperative if the patient is to have full advantage of the even chance that his tumor is completely removable.

The incidence of tumors of the spinal canal is highest from the fourth to the sixth decades. They are less common in childhood than in old age. Distribution as to sex is about equal.

Extramedullary Tumors.—With the favorable extramedullary tumors sensory changes are generally more pronounced in the distal parts of the extremities, and the saddle area and sphincters may be spared until late in the disease. Radicular pain is commoner and more intense with extramedullary tumors than with the intramedullary group. Occasionally these growths contain calcium and may be seen in plain roentgenograms of the spine; local change in the interpedicular space of the same or an adjacent vertebra may give a clue as to the location of the tumor.

Meningioma.—Of the encapsulated extramedullary tumors of the spinal canal, meningioma is the most commonly encountered; the incidence is higher in females than in males. It usually grows from the attachment of the dentate ligament and in its development may project on either side of this or may straddle it. The tumor can usually be dissected away from the cord if irritation has not stimulated too intimate an adhesive process. By removal of the dural attachment extirpation is usually possible. At times it is necessary to sacrifice nerve roots, however, to accomplish satisfactory end results.

Perineurial Fibroblastoma.—Perineurial fibroblastoma is the next most common encapsulated tumor of the spinal canal. This tumor arises from nerve roots and has a history similar to that of the meningioma. In its complete removal it is always necessary to sacrifice at least the root from which it springs.

Multiple cord tumors may be encountered in von Recklinghausen's disease. Perineurial fibroblastomas and neurofibromas may be found in this symptom complex, as well as intramedullary tumors of the glioma group. Usually only those tumors which are producing symptoms are removed; a condition in which many symptom-producing growths are present at one time is unusual in this fairly common disease of the nervous system.

Gliomas of the Spinal Cord.—Gliomas of the spinal cord include all of the types mentioned in discussion of gliomas of the brain. They may be primary or may arise from seedings floating into the spinal canal from mother gliomas in the cranium.

Medulloblastoma: Medulloblastoma is the glioma that most frequently gives rise to daughter spinal growths, but all the gliomas are reported to have been the source of spinal metastases.

Ependymoma: The most commonly observed primary spinal glioma is ependymoma, which arises in conjunction with the filum terminale or the central canal. It grows slowly and may have produced generalized widening of the interlaminal arches by the time it is recognized clinically, particularly when it originates in the filum terminale. These tumors are bluish purple in color and are usually moderately firm but may contain cystic collections. Occasionally in the early stages they may be completely removed, but when they have grown to incorporate the fibers of the cauda equina extensively, decompression and roentgen therapy give a better result than can be accomplished by radical surgical procedures.

Astrocytoma: Astrocytoma of the spinal cord is usually fibrous and cystic. It may extend over long areas of the cord and is sometimes mistaken for syringomyelia.

Glioblastoma multiforme: Glioblastoma multiforme has been described in the spinal cord but is rare in this location.

Gliomas of the spinal cord as a group are not surgically removable. The cord can be decompressed, however, and benefit can usually be anticipated from roentgen therapy.

Angioma.—Angioma of the spinal cord usually is of the cavernous type and progresses by altering the blood supply of the cord and by expansion of existing blood vessels. It is commonest in the cervical and upper thoracic regions. It is found from early childhood until late middle life. Dilatation of the existing channels may produce a block of the spinal canal, but angiomas may expand to considerable size without obstructing the canal. The myelographic picture of hemangioma outlining the tortuous vessels, particularly along the dorsal surface of the cord, is quite characteristic. Cystic changes in the adjacent portion of the spinal cord may be seen and are probably metabolic in character.

Epidermoid Cysts.—Epidermoid cysts of the spinal canal are most commonly encountered in the caudal region, where their slow growth exerts gradually increasing pressure on the roots of the cauda equina. They may appear anywhere along the spinal canal, however, and have been described within the spinal cord itself. Epidermoids of the cauda equina often can be completely removed. In the cord itself the outlook is less favorable, but with decompression and removal of the content of the cyst those fiber pathways not permanently damaged may be expected to recover.

Intrinsic Tumors of the Vertebrae.—Intrinsic tumors of the vertebrae may exert pressure on the spinal cord by direct extension. Hodgkin's tumors and lymphosarcomas may appear in the epidural space. Tumors may metastasize from any part of the body to the spine with secondary involvement by pressure of

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the spinal cord. Tumors of the breast and thoracic cage and of the kidney are particularly prone to do this.

Intervertebral Disk.—A group of symptoms indistinguishable from those of a neoplastic growth in the spinal canal can be produced by extrusion of degenerated intervertebral disk material, most frequently in the lumbar or in the cervical region. Protruding intervertebral disk material in the lumbar region usually impinges on and irritates roots of the lumbosacral area. The protrusion may be sufficient to block the spinal subarachnoid space and to produce symptoms of generalized compression. A similar situation can exist in the cervical region, where root or cord or both may be involved by protrusion of degenerated intervertebral disk material. Five per cent of lesions of the spinal canal operated on with a preoperative diagnosis of protruded intervertebral disk material prove to be neoplasms; and occasionally protruded disk material is encountered when a tumor was anticipated.

Other Vertebral Tumors.—Tumors arising in the vicinity of the vertebral column may project into the spinal canal through the intervertebral foramina and, conversely, certain neurofibromas and perineurial fibroblastomas may project out from the canal into the surrounding paravertebral region. These tumors, because they are constricted as they pass through the intervertebral foramen, are known as dumb-bell or hour-glass tumors. Roentgen films of the intervertebral foramina will usually satisfactorily demonstrate their enlargement. The intraspinal portion of the tumor compresses the cord as does any extradural or extramedullary tumor, and the problem as to both diagnosis and treatment is that of extramedullary tumors.

Granuloma.—Granuloma, particularly tuberculoma, and occasionally encapsulated extradural abscess may compress the spinal cord, interfere with its blood supply and produce generalized and irreversible changes unless, fortunately, it is recognized in an early stage.

Prognosis.—Successful removal of encapsulated tumors of the spinal canal is highly satisfactory. The operative mortality is low, and the results when surgical intervention has been possible at a sufficiently early date are most favorable. The results of surgical treatment in the intramedullary group are not as promising, but benefit may follow decompression and roentgen therapy.

After surgical treatment of both intramedullary and extramedullary tumors of the cord, it is most important to preserve the fullest possible range of activity in the joints of the affected extremities. Paralysis of the bladder demands particular care, since renal infection is prominent among the causes of morbidity and death following a lesion of the spinal cord. During periods of complete paralysis, whether permanent or transitory, prevention of decubitus ulcers must be emphasized.

TUMORS OF THE PERIPHERAL NERVES

Tumors of Nerve Sheaths.—Most of the tumors affecting peripheral nerves primarily are considered to be tumors of the nerve sheath rather than of the neuronal elements themselves. These tumors are usually benign and can be completely removed, or at worst they recur only locally. Certain malignant tumors of peripheral nerves do exist, however, and when found must be considered as exceedingly grave. Cancer, when present, is of an exceptionally high order.

Perineurial Fibroblastoma.—Perineurial fibroblastoma may arise in the peripheral nerves as well as in the cranium and in the spinal canal. Here as elsewhere the tumor arises from the perineurium and pushes aside the fibrous pathways as it enlarges, although occasionally fibers may become incorporated in its capsule. Growth is usually slow. There may be areas of fatty or cystic degeneration in the tumor, and its histologic characteristics seldom leave doubt as to its identity. The tumor usually can be enucleated without sacrifice of the nerve by splitting the overlying fibers.

In malignant perineurial fibroblastoma repeated recurrence of the tumor may necessitate local but radical extirpation, including the nerve and adjacent structures.

Neurofibromas.—Neurofibromas may appear in peripheral nerves. In this tumor the proliferating tumor cells incorporate the nerve fibers within their substance and often will already have throttled the function of the nerve to a more or less complete degree when first seen. Such tumors seldom occur as isolated growths and generally are part of the symptom complex of von Recklinghausen's disease. When removal does appear to be indicated, extirpation of the tumor necessarily requires excision of the involved portion of the nerve. Where possible the nerve ends are brought together; often the diffuse thickening of the nerve for long distances on either side of a neurofibroma will make it impossible to extirpate the growth satisfactorily.

Neurofibrosarcoma.—Neurofibrosarcoma is a highly malignant tumor of peripheral nerves. Usually the history is of sudden appearance of a tumor *de novo* or of recent enlargement of a previously existing one. A peripheral nerve tumor with a short history or with a history of rapid growth should be regarded as malignant, and when it is approached surgically the operation should be performed with the idea that amputation of the extremity may be necessary if the patient's life is to be saved. Frozen sections of such a tumor should be made at the time of the operation so that there will be no delay in radical treatment if malignancy is present.

Von Recklinghausen's Disease.—Von Recklinghausen's disease is a symptom complex associated with extensive involvement of the entire nervous system, central as well as peripheral. The most commonly recognized symptoms are peripheral in nature, however, and include café-au-lait spots and multiple subcutaneous nodules which are neurofibromatous in character. Neurofibromas and perineurial fibroblastomas of peripheral nerves are encountered as well as tumors of the nerve roots within the cranium and spinal canal and gliomas of the brain and spinal cord. Any symptoms suggestive of involvement of other portions of the nervous system, peripheral and/or central, in a patient with von Recklinghausen's disease must be regarded with particular attention; multiple lesions are the rule rather than the exception.

Tumors of the Neuronal Element.—Tumors of the neuronal element are extremely rare in peripheral nerves. Ganglioneuromas are usually found in the retroperitoneal or mediastinal spaces. Most frequently they are seen in childhood and infancy. Usually they are encapsulated and if completely removable do not tend to recur. Neuroepitheliomas, which fortunately are rare, are highly malignant and require radical treatment, including amputation if they are in a limb.

Clinical Notes, Suggestions and New Instruments

CONGENITAL TOXOPLASMOSIS

B. H. KEAN, M.D.
and
ROBERT G. GROCOTT, B.S.
New York

Toxoplasmosis has been clearly recognized as a disease of human beings only in recent years, but the disease is apparently much more prevalent than has been appreciated. Various clinical and pathologic types, congenital, infantile, adult typhus-like, chronic and asymptomatic, have been described. Since excellent reviews of this rather complicated subject have been provided by Wolf, Cowen and Paige,[1] Sabin,[2] Weinman,[3] Pratt-Thomas and Cannon,[4] Zuelzer[5] and, recently, Callahan, Russell and Smith,[6] another summary of the literature would be superfluous.

Summary of Results of Histologic Examination

Organ	Number of Blocks	Number of Slides	Slides Positive for Toxoplasma	Inflammatory Reaction
1. Cerebrum	5	5	2	++++
2. Brain stem	5	11	6	++++
3. Spinal cord	4	9	9	+
4. Eye, including optic nerve	2	35	3	++++
5. Nerve, 5th cranial	1	5	5	++++
6. Nerve, femoral	2	2	1	++
7. Lungs	7	7	0	+
8. Heart	4	16	0	+
9. Liver	4	4	0	0
10. Spleen	4	4	0	0
11. Pancreas	1	1	0	0
12. Thymus	1	1	0	0
13. Thyroid	2	2	0	0
14. Adrenal glands	4	4	0	0
15. Intestines	5	5	0	0
16. Kidney	3	3	1	0
17. Urinary bladder (in nerve)	3	3	1	++
18. Penis	1	2	0	+
19. Lymph nodes	3	3	0	0
20. Bone marrow	4	4	0	0
21. Bone and cartilage	2	4	0	0
22. Mammary gland	1	1	0	+
23. Nipple (in muscle)	1	1	1	+
24. Parotid gland (in muscle)	1	1	1	++
25. Ear	2	2	0	0
26. Lip	1	1	0	+
27. Larynx	3	3	0	+
28. Tongue	2	5	3	++
29. Skeletal muscle	7	11	9	+
30. Umbilical cord	2	2	0	0

REPORT OF CASE

Clinical Background.—On Oct. 6, 1945, the father brought to Gorgas Hospital an infant who had been delivered one and one-half hours earlier at home. The midwife, recognizing prematurity and stating that she had never seen such a "gray" placenta, insisted that the child be brought to the hospital.

On admission no abnormalities other than prematurity were recognized; examination purposely was limited. The child was placed in an incubator. He became cyanotic, respirations were gasping and irregular, and the infant died nine hours after admission, ten and one-half hours after birth. There were no convulsions. The placenta that had been carefully brought in

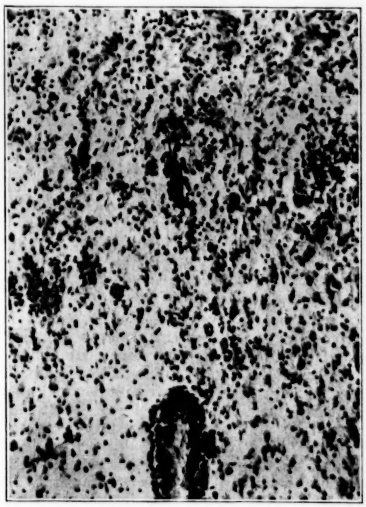

Fig. 1.—Section of cerebral cortex showing intense inflammatory reaction. × 175.

Fig. 2.—Individual parasites in brain. × 1,400.

From the Board of Health Laboratory, Gorgas Hospital, Ancon, Canal Zone, and the New York University College of Medicine.

1. Wolf, A.; Cowen, D., and Paige, B. H.: Toxoplasmic Encephalomyelitis, Am. J. Path. **15**: 657-694, 1939; Toxoplasmic Encephalomyelitis: Clinical Diagnosis of Infantile or Congenital Toxoplasmosis; Survival Beyond Infancy, Arch. Neurol. & Psychiat. **48**: 689-739 (Nov.) 1942.
2. Sabin, A. B.: Toxoplasmosis, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1943, vol. 4, chap. 7, pp. 43-54.
3. Weinman, D.: Human Toxoplasma, Puerto Rico J. Pub. Health & Trop. Med. **20**: 125-161, 1944.
4. Pratt-Thomas, H. R., and Cannon, W. M.: Systemic Infantile Toxoplasmosis, Am. J. Path. **22**: 779-795, 1946.
5. Zuelzer, W. W.: Infantile Toxoplasmosis, with a Report of Three New Cases, Including Two in Which the Patients Were Identical Twins, Arch. Path. **38**: 1-19 (July) 1944.
6. Callahan, W. P., Jr.; Russell, W. D., and Smith, M. C.: Human Toxoplasmosis, Medicine **25**: 343-397, 1946.

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with the child was rejected at the admitting office of the hospital and discarded.

The family, mother, father and their 20 month old son had lived for about ten months in Rio Abajo, a fairly well sanitated community about 7 miles (11.3 kilometers) from the City of Panama. Their house, of mixed wood and concrete construction, was located at the edge of the village not more than 50 yards (45.7 meters) from the "bush." Many less pretentious houses were in the neighborhood. Cats, dogs, goats, chickens, rats and pigeons were in the yard or close by. Mosquitoes were the bane of the neighborhood. No other insects were reported as troublesome, but most of the dogs were infested with Rhipicephalus sanguineus, the common dog tick. The family was admitted to the hospital for study.

The mother was a 24 year old Panamanian multipara. At the age of 16 years she had two abortions (each at three months), each by a different consort. Her next child (by the current husband) was now 20 months of age. The fourth was the infant with toxoplasmosis. Her last menstrual period started Feb. 18,

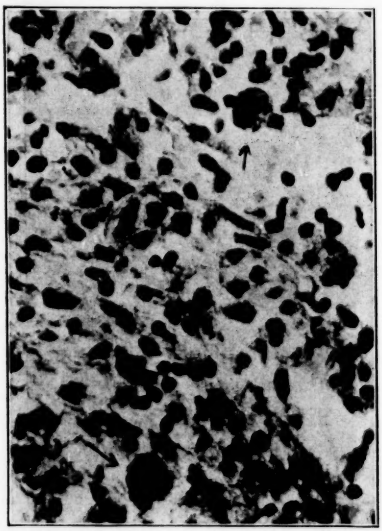

Fig. 3.—Section of fifth cranial nerve showing two nests of parasites. × 1,000.

1945. She felt perfectly well during her pregnancy. On October 6 she went into labor, and "a few hours" later was delivered without difficulty. The puerperium was uneventful. Physical examination, routine hematologic studies, urinalyses, stool examinations, ophthalmologic examination, electrocardiogram and roentgenograms of the skull and chest revealed no abnormality. The Wassermann reaction of the blood was negative; the Kahn reaction was positive.

The father was a 30 year old Colombian mestizo, who had lived in Panama for five years. He had a history of gonorrhea, inadequately treated syphilis, and vague fever several years previously. In other respects, the personal history, family history, physical examination, roentgenograms of the skull and chest and an electrocardiogram revealed no abnormality. A small patch of healed chorioretinitis was found "at 6 o'clock near the periphery of the right eye." Wassermann and Kahn reactions of the blood were positive.

The 20 month old son was in excellent health. Complete examination of a type similar to that conducted on the father revealed no abnormality. His fundi were normal.

Necropsy.—Gross Examination: Permission for autopsy could not be obtained until thirty-one hours after death. During this period the body was kept in the refrigerator at a temperature of 32 to 38 F.

Fig. 4.—Intense choroiditis. × 175.

Fig. 5.—Small nest of parasites in eye. × 1,400.

The infant weighed 1,070 Gm. and measured 38 cm. from vertex to heel. The estimated intrauterine age was 6½ to 7 months. The head appeared somewhat smaller than usual,

but its circumference was not measured. The fontanelles were flat.

When the calvarium was removed much bloody cerebrospinal fluid gushed forth. (In a test tube, after an hour, a thick layer of white, yellow and gray granular material settled to the bottom. The supernatant fluid was reddish brown and turbid.)

Fig. 6.—Section of spinal cord showing symmetric calcification. × 8.

Fig. 7.—Nest of parasites in spinal cord. ×1,400.

The brain was a collapsed, gelatinous, almost shapeless mass which lay on the floor of the middle cranial fossa and was covered by hemorrhagic leptomeninges, in portions of which yellowish zones were seen. On removal, the cerebrum was so soft that it could hardly be handled, and no statement can be made concerning the convolutional pattern. The tissue was pale, but flecked with conspicuous firm yellow granules. The cerebellum could not be identified even after long search.[7] The brain stem was firmer, and the pons and medulla were recognizable as such. The spinal cord was soft, but its identifying landmarks were discernible. Sectioning of the pons, medulla and cord disclosed gritty, yellowish areas, averaging 0.2 cm. to 0.3 cm. in diameter; they showed a tendency to symmetry in location. The pituitary was of average size. The pattern of the skull appeared normal.

The lungs were atelectatic. All other organs seemed normal on gross examination.

Histologic Examination (the table): Brain. Scattered in the cortex and brain stem were many areas of focal necrosis with an intense granulomatous inflammatory reaction featuring an infiltration of macrophages, lymphocytes and plasma cells. In the areas of necrosis was an extensive deposition of calcium salts that could be demonstrated beautifully by the von Kossa stain. In the brain stem the zones of necrosis tended to be symmetric, but in the cerebral hemispheres no pattern could be discerned and in some areas there was a diffuse inflammatory

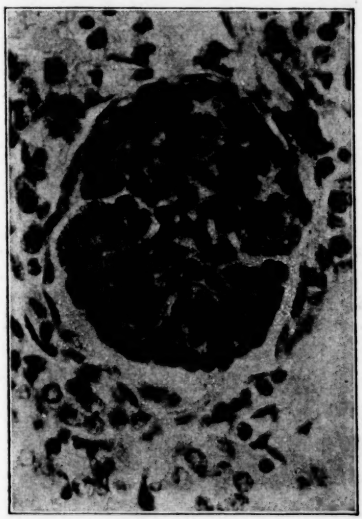

Fig. 8.—Nest of parasites in glomerular tuft. × 1,200.

reaction in addition to the focal one. A moderately intense leptomeningitis was present and some blood pigment was noted in macrophages scattered in the meshes of the pia-arachnoid. Toxoplasmas disposed singly, in small groups and in pseudocysts were found without prolonged search. The individual parasites averaged 5 microns in length and 1 micron in width. In the spinal cord the inflammatory reaction was slight, but the parasites were seen in sections from cervical, thoracic and lumbar levels.

Eye. An intense granulomatous chorioretinitis was present. Parasites were few and could be found only after prolonged search, as small cystlike aggregates of three or four toxoplasmas.

Optic nerve. No parasites were seen, although an inflammatory reaction was present.

Fifth cranial nerve. Many toxoplasmas and an intense inflammatory reaction were seen.

7. How much of the necrosis and collapse of the cerebral hemispheres was ante mortem and how much was post mortem was difficult to ascertain. The absence of cerebellum and the fact that in many instances in which autopsies had been done on infants in similar circumstances no such complete collapse had been seen suggested strongly that most of the changes were ante mortem.

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Lungs. Moderate atelectasis and a slight inflammatory reaction were noted. No parasites were found. Evidence of congenital syphilis was not recognized.

Heart. A barely recognizable diffuse inflammatory reaction was present. No parasites were seen.

Liver. No parasites were noted. There was no evidence of congenital syphilis.

Kidneys. Caught within glomerular tufts were a few small nests of toxoplasmas that had excited no inflammatory reaction.

Bladder. In the lamina propria of the mucosa and in the muscular layers was a diffuse inflammatory reaction. Several small nests of toxoplasmas were found in nerve bundles.

Mammary gland. No parasites were seen in a section of the gland. In the adjacent skeletal muscle toxoplasmas were present.

Parotid gland. The glandular elements appeared normal. In adjacent skeletal muscle toxoplasmas were seen.

Fig. 9.—Nest of parasites in bladder. × 1,400.

Tongue. Several groups of toxoplasmas were present. The inflammatory reaction was moderate.

Skeletal muscle (leg and back). Toxoplasma pseudocysts were relatively numerous.

Femoral nerve. Many toxoplasmas and an intense inflammatory reaction were present.

Thymus, thyroid, spleen, pancreas, adrenal glands, intestine, lymph nodes, bone marrow and umbilical cord. No lesions or parasites were seen.

Experiments.—Infant: Guinea pigs inoculated intraperitoneally with emulsions of brain suspended in the hemorrhagic spinal fluid died in ten days. Toxoplasmas were easily demonstrated in the peritoneal exudate, in the brain and many other organs of these guinea pigs. Toxoplasmas recovered from these pigs were lethal on subinoculation to other guinea pigs, and the strain was carried through several series of guinea pigs. (It is of interest that the parasites were viable after thirty-one hours in the refrigerator at a temperature of 32 to 38 F.)

Mother: Spinal fluid, venous blood, cervical and vaginal washings, all taken from the mother ten days after delivery, were injected into the peritoneal cavity of guinea pigs but failed to infect them. No toxoplasmas were seen in thick films of this material or in her breast milk. No parasites were found in 150 sections of a biopsy of her deltoid muscle taken

Fig. 10.—Nest of parasites in skeletal muscle of tongue. × 350.

Fig. 11.—Nest of parasites in skeletal muscle of leg.

at the same time. An emulsion prepared from crushed deltoid muscle was injected into guinea pigs, and produced no infection.

Father: Venous blood failed to infect guinea pigs inoculated intraperitoneally. No parasites were seen in thick films of his prostatic fluid.

COMMENT

Pratt-Thomas and Cannon [4] listed 20 previously noted cases of toxoplasmosis confirmed by autopsy and added 1 of their own. Callahan, Russell and Smith [6] recently added 5 cases in infants. The case reported here, therefore, is the twenty-seventh proved by necropsy and the twenty-first in an infant. This is the first proved case of congenital toxoplasmosis on the Isthmus of Panama, although 5 other cases of toxoplasmosis have been seen.[8]

The absence of any symptoms of the disease in the mother was perplexing as usual. It is reasonable to assume that the infection of the fetus occurred rather late in the pregnancy, and yet the mother remembered no illness. Efforts to demonstrate a latent infection in maternal body fluids and skeletal muscle were unsuccessful.

The number of organs involved in this and other cases [9] indicated that toxoplasmosis is a systemic disease with a predilection for the central nervous system but the ability to appear in almost any organ. The parasitization of nerves (fifth, cranial, femoral and nerves in bladder) has not been described previously in human beings to the best of our knowledge. Johnson,[10] however, recorded extensive involvement of nerves in toxoplasmosis in pigeons.

The widespread incidence of toxoplasmosis in animals [11] and the relative lack of host specificity of the parasite suggest that human infection occurs by transmission of the disease from an animal reservoir. Although transmission may be direct, the possibility of the existence of an insect vector must be considered. Since the disease has been described in various parts of the world, it is unlikely that either the animal reservoir or the insect vector—if they exist—is exotic. On the basis of very little evidence we would like to suggest the possibility that pigeons may play an important role. Johnson [10] described an epidemic of toxoplasmosis in carrier pigeons in the Canal Zone, and pigeons were noted close to the home of the patient described in the current case report. These birds were also seen in the neighborhood of the homes of 2 patients with asymptomatic toxoplasmosis on the Isthmus of Panama. (Departure of one of us, B. H. K., from the Canal Zone prevented further investigation of this possibility.) Mosquitoes might qualify as a vector.

Parenthetically, the occurrence of severe congenital encephalomyelitis in another male infant, stillborn after six months of intrauterine life, should be mentioned. In this infant, the cerebral hemispheres were small, soft, collapsed and covered by reddish brown leptomeninges. Histologically an intense granulomatous inflammatory reaction similar to that seen in the current case of toxoplasmosis was present. Parasites were not demonstrated, however, either visually or by guinea pig inoculations; nevertheless we believe that this might well represent a "burnt-out" case of toxoplasmosis.

SUMMARY

A case of toxoplasmosis, the twenty-seventh authenticated by autopsy, the twenty-first in an infant and the first of the congenital type on the Isthmus of Panama, is reported. Parasites were found in the brain, spinal cord, eye, fifth cranial nerve, femoral nerve, kidney, urinary bladder nerves and skeletal muscles of the tongue, cheek, chest, leg and back. Attempts to demonstrate a latent infection in the mother were unsuccessful. On extremely tenuous grounds the possibility is suggested that pigeons may act as an animal reservoir.

8. Kean, B. H., and Grocott, R. G.: Asymptomatic Toxoplasmosis, Am. J. Trop Med., to be published.
9. Weinman,[8] Zuelzer,[5] Callahan, Russell and Smith.[6]
10. Johnson, C.: Annual Report of the Gorgas Memorial Laboratory, 1943, Washington, D. C., Government Printing Office, 1944, pp. 15-16.
11. Manwell, R. D.; Coulston, F.; Binckley, E. C., and Jones, V. P.: Mammalian and Avian Toxoplasmosis, J. Infect. Dis. **76:** 1-14, 1945.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following reports. HOWARD A. CARTER, *Secretary.*

IMPROVED NEBULIZER PREMO ACCEPTABLE

Manufacturer: Premo Pharmaceutical Laboratories, Inc., 443 Broadway, New York 13.

The Improved Nebulizer Premo is a device, mainly of glass, for projecting liquids, especially aqueous solutions, as extremely fine mists, or aerosols. This makes it possible to administer by inhalation nonvolatile medicaments, like epinephrine and penicillin. The construction of the device is such that practically all of the liquid placed in it may be nebulized.

Improved Nebulizer Premo.

The Council on Pharmacy and Chemistry has accepted a preparation of penicillin for administration by this method. There is evidence that a patient who inhales, for instance, 50,000 units of penicillin will show a concentration of 0.1 to 0.2 units of penicillin per cubic centimeter of serum for a period as long as two hours after the inhalation.

Because of the fineness of the division of the nebulized liquid, the process of administration is not fast. One cubic centimeter of water required four and one-half minutes to be completely nebulized when compressed air was used and required seven minutes by manual employment of the rubber bulb.

The Council voted to include the Improved Nebulizer Premo in its list of accepted devices.

OTARION HEARING AID MODEL E1, ACCEPTABLE

Manufacturer: Otarion Hearing Aids, 448 North Wells Street, Chicago 10.

This instrument is a self-contained hearing aid, with the battery compartment at the lower end of the case. The case is a die-cast magnesium alloy, coated with Vinyl Resin finish. A side-hinged full-length back cover gives access to the batteries and the two tubes, which are not covered. One magnetic type receiver is used and is connected to the amplifier by means of a plastic-covered cord with plugs at both ends.

Two wheel-type controls are placed on the top of the case. One is a volume control. The other is a combination on-off tone control having an off position and three tone positions. A detachable wearing clip fastens to the back of the case.

Dimensions and Weight

Dimensions: 130 by 67 by 22 mm. (5⅛ by 2⅝ by ⅞ inch).

Weight: Approximately 219 Gm. (7½ ounces) (with batteries).

Battery Drain Data	Measured Voltage	Measured Current
A, zinc and carbon, 1.5 volts.....	1.3 volts	55 milliamperes
B, zinc and carbon, 30 volts (Quiet)....	29 volts	0.46 milliampere
(Squealing)	29 volts	0.4 milliampere

Acoustical Gain

Measurements were made of the acoustical gain in decibels (sound pressure in 2 cc. coupler in decibels above sound pressure at microphone, with microphone set in 30 by 20 cm. baffle) with the input level held at 0.02 dyne per square centimeter.

The following tabulation gives typical results obtained with the volume control full on, for two settings of the tone-control at each of seven frequencies:

Frequency	256	512	1,024	1,200	2,250	3,100	4,096	cycles
Tone: 1 dot.....	33	36	41	51	40	32	17	db.
Tone: 3 dots.....	22	30	41	50	40	32	17	db.

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Approximate values of maximum sound pressure levels at four frequencies observed in the 2 cc. coupler with volume set for full gain and tone setting "1 dot" are shown below:

Frequency	Input Level	Maximum Output Level
600 cycles	65 decibels	103 decibels
1,024 cycles	70 decibels	111 decibels
1,200 cycles	70 decibels	114 decibels
2,048 cycles	65 decibels	100 decibels

Intelligibility tests (random words) were made with a person of normal hearing seated inside a booth giving about 30 decibels sound reduction. The speaking person was outside the booth using a normal tone of voice. Score made under these critical conditions was 40 per cent. The instrument was quiet, but low amplification caused the low score. It appeared that the instrument would be satisfactory for subjects requiring moderate amplification. It could not be recommended in severe cases of deafness.

On the recommendation of the Consultants on Audiometers and Hearing Aids, the Council on Physical Medicine voted to include the Otarion Hearing Aid, Model E 1, in its list of accepted devices.

PARAVOX HEARING AID, MODEL XTS, ACCEPTABLE

Manufacturer: Paraphone Hearing Aid, Inc., 2056 East Fourth Street, Cleveland 15.

This self-contained hearing aid comes in a plastic-coated metal case, with the battery compartment at the lower end of the case. Access to the batteries is made possible by a sliding cover plate half the length of the instrument. The amplifier remains well protected in the upper half of the case when the battery cover is removed. A crystal type receiver is connected to the amplifier by means of a 76 cm. (30 inch) plastic covered cord, with plugs at each end.

Paravox Hearing Aid, Model XTS.

There are two wheel-type control knobs on the top of the instrument, one to regulate the volume and the other to select the tone (three positions) and turn off the aid. A wearing clip is fastened to the front of the case directly above the microphone.

Dimensions and Weight

The dimensions are 127 by 63 by 19 mm. The weight (with batteries) is approximately 173 Gm. (6 ounces).

Battery Drain Data	Measured Voltage	Measured Current
A: Zinc-carbon, 1.5 volts.....	1.4 volts	40.00 milliamperes
B: Zinc-carbon, 30 volts (Quiet)....	29.0 volts	0.60 milliampere
(Squealing)	29.0 volts	0.60 milliampere

Acoustical Gain

Measurements were made of the acoustical gain in decibels (sound pressure in 2 cc. coupler in decibels above sound pressure at microphone, with microphone set in 30 by 20 cm. baffle) with input level held at 0.02 dyne per square centimeter.

The following tabulation gives typical results obtained with the volume-control full on, for two settings of the tone control at each of seven frequencies:

Frequency.....	256	512	1,024	1,200	2,250	3,100	4,096 cycles
Tone: 1 dot.....	45	58	66	69	48	61	58 decibels
Tone: 3 dots.....	30	43	52	55	29	38	35 decibels

Approximate values of maximum sound pressure levels at four frequencies set up in the 2 cc. coupler were determined with the volume set for full gain and tone setting at one dot:

Frequency	Input Level	Maximum Output Level
600 cycles	60 decibels	114 decibels
1,024 cycles	60 decibels	120 decibels
1,200 cycles	60 decibels	123 decibels
2,048 cycles	60 decibels	103 decibels

Intelligibility tests of random words were made with a person of normal hearing seated inside a booth giving about a 30 decibel reduction in sound. The speaking person was outside the booth using normal speaking voice. The score made under these critical conditions was 61 per cent.

On the recommendation of the Consultants on Audiometers and Hearing Aids, the Council on Physical Medicine voted to include the Paravox Hearing Aid, Model XTS, in its list of accepted devices.

MICROTONE AUDIOMATIC HEARING AID MODEL T 4 ACCEPTABLE

Manufacturer: The Microtone Company, 4602 Nicollet Avenue, Minneapolis 9.

The Microtone Audiomatic Hearing Aid, Model T 4, is a plastic-cased, self contained instrument with the battery compartment at the lower end of the case. Half of the back is removable for access to the battery and is secured by a snap catch. A crystal receiver is connected to the instrument by a plastic-covered cord.

A three position lever switch at an upper corner of the instrument has an off position and two tone positions. The wheel-type volume control is at the other upper corner of the case. The wearing clip is at the center on the front of the case.

Dimensions and Weight.—Dimensions 127 by 64 by 25 mm. Weight (with batteries) 255 Gm. (9 ounces).

Batteries (Zinc and Carbon)	Measured Voltage	Measured Current
A 1.5 volts.....	1.3 volts	46 milliamperes
B 30 volts (Quiet)....	29 volts	0.4 milliampere
(Squealing)	29 volts	0.5 milliampere

Microtone Audiomatic Hearing Aid Model T-4

Acoustical Gain.—Measurements were made of the acoustical gain of the instrument in decibels. This is the decibel difference in sound pressure between the pressure at the face of the microphone opening (with instrument set in 40 by 20 cm. baffle) and the pressure produced by the receiver in a 2 cc. coupler. The microphone sound pressure was held at a level 40 decibels above 0.0002 dyne per square centimeter. Following is a tabulation of typical results in decibels:

Frequency	256	512	1,024	1,200	2,250	3,100	4,096
Tone-control "up".....	30	41	54	57	49	47	43
Tone-control "down"....	25	32	51	55	44	45	38

Maximum Output Pressure.—Measurements were made of the approximate maximum sound pressures the instrument would produce in the 2 cc. coupler with the instrument set for full gain and "up" tone position. Levels are in decibels relative to 0.0002 dyne per square centimeter. Results are shown below:

Frequency	Input Level	Maximum Output Level
600 cycles	65 decibels	107 decibels
1,024 cycles	65 decibels	117 decibels
2,048 cycles	65 decibels	102 decibels
2,750 cycles	65 decibels	111 decibels

Intelligibility tests (random words) were made with a person of normal hearing seated inside a booth giving a sound reduction of about 30 decibels. The speaking person was outside the booth using a normal tone of voice. The score made under these critical conditions was 30 per cent. Instrument background noise caused the low score. A deafened person should attain much better results.

On the recommendation of the Consultants on Audiometers and Hearing Aids, the Council on Physical Medicine voted to include the Microtone Audiomatic Hearing Aid, Model T-4, in its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JANUARY 10, 1948

THE ETIOLOGY OF APICAL SCARS

Fibrous scars accompanied regularly by local anthracosis and emphysema and sometimes by fibrotic, caseous or calcific nodules are commonly found at necropsy in the apexes of one or both lungs. These have long been accepted as tuberculous scars. This interpretation has recently been challenged by Medlar,[1] whose data warrant critical examination before the old concept is discarded.

Medlar analyzed data on 1,400 necropsies in cases of unexpected death in the Medical Examiner's Department of the Borough of Manhattan. Of this number, 141 were excluded from further consideration because of extensive pleural or pulmonic disease. The 1,259 remaining cases, in which 960 subjects were white and 299 were Negro, were analyzed according to race, age and apical scars in relation to presence or absence of tuberculous lesions. Calcified or caseous foci or tuberculous cavity in the lung, or similar lesions elsewhere, were accepted as diagnostic of tuberculosis.

Apical scars were present in 48.1 per cent of white subjects who had evidence of tuberculosis and in 31.9 per cent of those without tuberculous lesions; the corresponding figures for Negroes were 14.7 and 8 per cent. The apical scars were related to age; none were found in 106 persons under 20 years of age; 65.9 per cent of 290 persons over 60 years of age had scars. The corresponding figures for tuberculous lesions in these two groups were 21.7 and 88 per cent. The apical scars were commoner in white persons than in Negroes at corresponding ages, and commoner in men than in women. They were bilateral in 97.2 per cent. Tuberculous foci were found contiguous to or in apical scars in 33 cases. In addition, 20 persons who had apical tuberculous lesions had no apical scars. Forty-five persons had apical tuberculous lesions but were excluded from the analysis because they had dense pleural adhesions.

1. Medlar, E. M.: Apical Scars; Their Etiological Relationship to Tuberculous Infection, Am. Rev. Tuberc. **55**: 511 (June) 1947.

Two separate questions are at issue: (1) Are the apical scars tuberculous and, if so, (2) are they the result of a postprimary hematogenous dissemination of tubercle bacilli or of infection by some other method?

Rejection of the tuberculous causation for the apical scars was based on five points: (*a*) Apical scars occurred as frequently in persons without evidence of tuberculous lesions as they did in those with tuberculous foci. (*b*) The bilateral and symmetric pattern of the apical scars bore no resemblance to the asymmetric and scattered distribution of the tuberculous lesions. (*c*) Tuberculous lesions occurred in the apex with or without apical scars being present. (*d*) Apical scars occurred in lower lobes only when they occupied an apical position, although tuberculous foci were found in the upper portion of the lower lobes when they occupied their normal site. (**e**) The differences noted in relation to sex and race were not accounted for by acceptance of a tuberculous etiology.

The incidence of tuberculous lesions (75.2 per cent in whites and 61.5 per cent in Negroes) was considerably less than that recently reported from Baltimore[2] (90 per cent) and from Chicago[3] (88.8 per cent). This may indicate that some tuberculous lesions were overlooked; special methods of detection were not used as in the latter two reports. The data in table 1 of Medlar's article show a parallelism between the incidence of apical scars and tuberculous lesions. Thus, 48.1 per cent of white persons with tuberculous lesions had apical scars and only 31.9 per cent of those without tuberculosis had the scars. The figures for Negroes were similar although lower. The bilateral and symmetric pattern of the apical scars in contrast to the asymmetric and scattered distribution of the tuberculous lesions does not disprove the tuberculous nature of the former. Many of the latter, no doubt, were the residues of primary infections which are known to be widely scattered in the lungs. Some of the tuberculous lesions in the apex without accompanying scars might, on microscopic examination, be found to be evolving to apical scars. Factors of time, resistance, exact site of infection and proximity of the lesion to the pleura might determine the type of anatomic lesion which would eventually result. The observation that apical scars occur in the apexes of lower lobes when they are elevated to form part of the dome of the lung speaks for a common etiologic basis rather than a different one. The sex difference in incidence of apical caps parallels, although at a lower level, those seen in tuberculous lesions. Factors of resistance or susceptibility might explain the differences noted in the racial groups as well as in the sexes.

2. Carnes, W. H.: The Present Incidence of Tuberculous Infection, Bull. Johns Hopkins Hosp. **70**: 101 (Feb.) 1942.

3. Steiner, P. E.; Stanger, D. W.; Bolyard, M., and Marcovich, A. W.: The Quantity of Focal (Tubercle) Calcium in Human Lungs, Am. Rev. Tuberc. **49**: 129 (Feb.) 1944.

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The theory that the apical scars are the result of a postprimary hematogenous dissemination of tubercle bacilli was rejected because it did not explain the presence of bilateral apical scars in cases which exhibited no tuberculous lesions. Perhaps tuberculous lesions in these cases had virtually disappeared or, as has been suggested, had been overlooked.

Careful consideration must be given to definition of the apical scar. Is it to be defined in the restricted sense of an anthracotic, fibrous scar confined to the pleura, or may it include also diffuse fibrous and even nodular caseous and calcific lesions immediately beneath the pleura? On microscopic sections made through the apexes a clearcut distinction is often impossible; the lesions merge into each other with respect to location, histologic type and stage of evolution. Scars in the apical pleura frequently show evidence that subjacent pulmonic tissue together with its lesions has been retracted and incorporated into the scar.

Possibly this problem cannot be solved by statistical methods, but it might yield to morphologic or experimental studies.

EXOTIC DISEASES

In this issue of THE JOURNAL, page 81, appears a case report by Levy and Yiengst [1] of kala-azar in New York City. This patient had been away from endemic areas of visceral leishmaniasis for seventeen to nineteen months, an incubation period not unusual in this disease. Preliminary physical examination revealed vague abdominal tenderness, loss in weight, fever and mild reddening of the pharynx but was otherwise negative. Observations of this sort might easily indicate any one of many other maladies common to the United States. Fortunately in this case the necessary medical curiosity combined with excellent laboratory facilities determined correct diagnosis and provided for proper treatment.

Without typical symptoms, differential diagnosis included consideration of malaria, leukemia, bacillary dysentery, typhoid, paratyphoid, undulant fever, typhus, tularemia and others. Diagnosis became apparent only after the second biopsy of bone marrow. Adequate laboratory facilities such as are implied in the foregoing account are not available to all practicing physicians in this country. Nevertheless exotic disease must now be constantly suspected.

In World War II several million Americans were transported beyond the limits of the United States, many hundreds of thousands to areas where tropical disease and diseases foreign to this country are endemic. Moreover, postwar civilian and military travel to these areas has greatly expanded.

Meleney,[2] Sawyer,[3] Mackie,[4] Faust [5] and many others have warned repeatedly of the danger of tropical disease occurrence in the United States. Diseases probably most frequently met will be malaria, bacillary dysentery, amebiasis, filariasis and intestinal protozoan infestations. These will be seen in areas where they were formerly rarities or nonexistent. Others, such as kala-azar, African and South American trypanosomiasis, cutaneous leishmaniasis, schistosomiasis, yaws and pinta will occur in scattered numbers. Prevalence of leprosy in areas where troops were stationed makes appearance of a few cases after long incubation periods almost inevitable.

Velocity plane travel which allows passengers to travel half around the world from home to destination within the intervals of short incubation periods in part nullifies usual quarantine methods and may allow entrance of patients with yellow fever, plague, cholera and epidemic typhus. Authorities in international health work have indicated that protection for the United States demands lowering of the incidence or stamping out of these communicable diseases in the endemic areas of the world. Effective work of this nature is now being done by the Rockefeller Foundation and in this hemisphere by the Health and Sanitation Division, Institute of Inter-American Affairs.

Most exotic diseases do not constitute epidemic or endemic hazards in the United States because known vectors or intermediate hosts are lacking and high standards of community sanitation prevail. The possibility exists, however, that new appropriate vectors and intermediate hosts may develop and that more virulent strains of the pathogens now common to this country may be imported.

Despite all epidemiologic considerations these diseases are immediate problems to the practicing physician. Proper cure of the patient and primary protection of the community will depend on the physician's diagnostic ability. Accurate typical clinical pictures are given by Strong [6] and other authors. However, many of the diseases mentioned, such as amebiasis, schistosomiasis, malaria and Chagas' disease, having passed through the acute stage and entered on a mild intermediate or chronic stage, present themselves in the patient in masked form. Symptoms are frequently vague, such as fatigue, recurrent headache, loss in weight, nervousness, palpitation and uneasiness with mild to moderate gastrointestinal distress. In view of the added stress placed in recent years on the

1. Levy, M. D., and Yiengst, M. J.: Kala-Azar: Report of a Case Showing Unusual Leukocyte Response and Prolonged Incubation Period, J. A. M. A. **136:** 81 (Jan. 10) 1948.

2. Meleney, H. E.: The Problem of Certain Tropical Diseases in the War, New England J. Med. **227:** 159-162 (July 30) 1942; Problems of Treatment of Tropical Diseases in Returning Military Personnel, New York State J. Med. **44:** 2105-2108 (Oct. 1) 1944.

3. Sawyer, W. A.: Public Health Implications of Tropical and Imported Diseases, Am. J. Pub. Health **34:** 7-14 (Jan.) 1944.

4. Mackie, T. T.: War and the Migration of Tropical Diseases, J. A. M. A. **122:** 1-4 (May 1) 1943; Tropical Diseases—a Postwar Health Program, New York State J. Med. **43:** 1509-1513 (Aug. 15) 1943.

5. Faust, E. C.: The Medical Aftermath of Global War, Mod. Hosp. **61:** 108 (Sept.) 1943.

6. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, Philadelphia, P. Blakiston's Son & Co., 1942.

psyche and the fact that these same symptoms are frequently met in psychoneurotic patients, differential diagnosis becomes doubly interesting, challenging and difficult.

Current Comment

ADVERTISING AIDS TUBERCULOSIS CAMPAIGN

Early in 1948 the Advertising Council, Inc., will be sponsoring a "Check Tuberculosis" campaign. The project has been undertaken in cooperation with the National Tuberculosis Association, its state and local affiliates, and the U. S. Public Health Service. The purpose of this campaign is educational. During the war the Advertising Council, Inc., aided the government in its campaigns for the sale of war bonds, for recruitment of nurses and in many health projects. Now all the various advertising technics will be utilized to emphasize the importance of early diagnosis in tuberculosis and to urge people to have the chest examined with the roentgen ray periodically. Tuberculosis is the first disease to be selected by the Advertising Council, Inc., as a target for a campaign, the reason being that we now possess the necessary technics and methods to eliminate this disease if only all the forces available can be mobilized against it.

EXPERIMENTAL STUDY OF STREPTOMYCIN DOSAGE IN TUBERCULOSIS

On the basis that streptomycin acts as an "antiseptic" chemical retardant, dosage has been computed on the assumption that the action of streptomycin in vitro is dependent on direct concentration and in vivo is likewise dependent on the concentration apparently reaching the tubercle bacillus. Toxic symptoms from the use of streptomycin in man were considered unavoidable. Recent observations in animals, on which such tests can be performed in a controlled manner, reveal that streptomycin produced the same effects in prolonging the lives of these animals against an otherwise lethal infection when given once in five days as when given every day. This is called the "remote sustained threshold action" of streptomycin [1] and includes all its implications as far as treatment of tuberculosis is concerned, even though it is admitted that the apparent action of streptomycin is neither clearly nor fully understood at present. However, one fact appears certain: Whatever beneficial effect streptomycin has on human tuberculosis may be obtained without forcing the use of this antibiotic to the point of injury to the patient. An adequate proving ground for claims that any product used may benefit the tuberculous patient has not been established; the hopes of the tuberculous person rise and fall with each pronouncement. More fundamental scientific information on streptomycin, or any alleged therapeutic agent against tuberculosis, is urgently needed—and soon!

1. Corper, H. J., and Cohn, M. L.: The Remote Sustained Threshold Therapeutic Action of Streptomycin in Tuberculosis, Science **106:** 446-447, 1947.

FLUORINE AND DENTAL CARIES

Since fluorine was discovered in drinking water [1] and identified as the causative agent for mottled enamel,[2] many reports have appeared showing the widespread distribution of areas of endemic fluorosis. The positive correlation between a concentration of fluorine in potable water of 1 part per million or more and mottled enamel of the teeth of children consuming this water since early infancy has been established. However, the fact that fluorine may have an other than deleterious effect on the teeth of children was first suggested in this country by Dean,[3] who commented on the rarity of dental caries in those areas where endemic fluorosis exists. Later,[4] on the basis of dental examinations of over 7,000 children in twenty-one cities, the conclusion was reached that there exists a general inverse relationship between the fluorine in the drinking water and the caries rate in children continuously consuming the water throughout life. Moreover, Klein [5] reported that this influence of fluorine can be demonstrated in children who have been exposed to drinking water containing this element for the first time, after reaching school age. There are indications [6] that the inhibiting effects of fluorine on dental caries can be demonstrated for a long time after removal of the element from the water supply. Furthermore, the suppression of the count of Lactobacillus acidophilus likewise endured. This organism was early implicated [7] in the causation of dental caries; later it was shown [8] that fluorine in such concentrations as occur in some potable waters suppresses acid production by the organism though not necessarily inhibiting its growth. A study of the available evidence led McClure [9] to state that from 0.5 to 1 part per million of fluorine in the drinking water is instrumental in reducing caries and that the evidence does not indicate that this constitutes a health hazard. The neighboring cities Newburgh and Kingston, N. Y., both originally used water low in fluorine. In 1944 the addition of 1 part per million of fluorine to the water supply was begun in Newburgh but not in Kingston. Recently, a report [10] compared the acidophilus count in the saliva of a large number of children 12 to 14 years of age in both cities with that before the experiment was begun. In Kingston the frequency of high and low counts remained in 1947 as it was in 1944; in Newburgh a progressive drop in the frequency of high counts and an increase in the proportion of low counts had occurred, thus indicating results in the direction of suppressing the acid-producing organisms in the mouth. Additional significant data are eagerly awaited from this study; further favorable results will mark progress in conquering a most vexing medical problem.

1. Churchill, H. V.: J. Indust. & Engin. Chem. **23:** 998, 1931.
2. Smith, M. C.; Lanz, E. M., and Smith, H. V.: Technical Bulletin 32, University of Arizona Agricultural College, 1931.
3. Dean, H. T.: Pub. Health Rep. **53:** 1443, 1938.
4. Dean, H. T.; Arnold, F. A., Jr., and Elvove, E.: Pub. Health Rep. **57:** 1155, 1942.
5. Klein, H.: Pub. Health Rep. **60:** 1462, 1945.
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7. Bunting, R. W.; Crowley, M.; Hard, D. G., and Keller, M.: Dent. Cosmos **70:** 1002, 1928.
8. Bibby, B. G., and Van Kesteren, M.: J. Dent. Research **19:** 391, 1940.
9. McClure, F. J.: Ingestion of Fluoride and Dental Caries, Am. J. Dis. Child. **66:** 362 (Oct.) 1943.
10. Finn, S. B., and Ast, D. B.: Science **106:** 292, 1947.

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ORGANIZATION SECTION

Miscellaneous

A CABINET DEPARTMENT OF HEALTH, EDUCATION AND SECURITY

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(This article has been approved by the Bureau of Legal Medicine and Legislation of the American Medical Association.)

Overshadowed by more spectacular legislation, the proposal to create a cabinet department to administer the health, education, public welfare and social security functions of the federal government has received little attention. A bill for this purpose, S. 140, was introduced early in the 80th Congress by Senators Fulbright and Taft. The proposal is in line with the steady increase in federal participation in fields which have in the past been largely the concern of state and local agencies. The bill in itself adds no new federal functions and grants no new authority, but it would add prestige to existing functions by giving them status in the highest level of government: the President's cabinet. In this connection it may have great potential significance.

STATE AND FEDERAL RELATIONSHIPS IN HEALTH, EDUCATION AND SECURITY

The Constitution gives Congress and the federal government the power "to promote the general welfare," but it has been generally understood that health, education and security functions are left for the most part to state and local authorities. Under the general welfare clause the federal government has gradually increased its activities in social fields in a rather haphazard, largely unplanned fashion. Legislation for this purpose tends to take two major forms, (1) expanding services performed by federal agencies and (2) increasing federal participation by grants-in-aid to the states for designated uses. Usually the promise of federal funds has been conditioned on requirements for matching state and/or local expenditures. Indeed, federal legislation has often had the deliberate purpose of stimulating state expenditures which probably would not have been made without this incentive. As a result, both state and federal governments have steadily increased their functions in health, education and security fields, and there is no evidence of any change in this trend.

The result of a succession of piecemeal legislation is that the relationship between federal and state-local responsibility has become hazy. It is not clear where local responsibility leaves off and federal responsibility begins. While the states tend to be jealous of federal encroachment, at the same time they are glad to receive federal funds. It may be worth while to consider briefly the present status of federal-state relationships in these activities.

WHAT IS THE PRESENT ROLE OF THE FEDERAL GOVERNMENT?

In the field of education state and local jurisdictions still carry the major share of responsibility. The federal role, although increasing, is still relatively minor. It is possible that federal participation in education may increase further, particularly in the poorer states which have yet to provide adequate educational facilities for their students. So far, however, federal activities in education are confined largely to compilation of school statistics, research and advisory services, and to grants-in-aid to states and private institutions for limited special purposes, such as vocational education, training of handicapped persons and scientific research (chart 1).

The federal role is greater in the field of health. There is, of course, an extensive federal medical program for the military services and veterans, but the U. S. Public Health Service is the major agency providing health services for the general public. While this agency is primarily concerned with research and disease prevention, successive legislation has increased its scope of activities for specific health problems: venereal disease, cancer and tuberculosis control, mental illness, hospital construction, etc. In addition, the Children's Bureau has health functions relating to problems of children, notably the administration of federal grants for maternal and child health, child welfare and services to crippled children. While the states have expanded their health services, they have come to be increasingly dependent on grants from the Public Health Service and the Children's Bureau (chart 2).

However, it is in the field of public assistance and social security that the federal government looms largest in the picture. Under the Social Security Act of 1935 the states were induced by the promise of federal matching grants to adopt or extend "categorical" programs of public assistance: old age

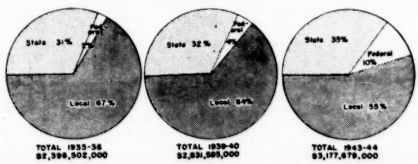

Chart 1.—Governmental expenditures for education by source of funds and fiscal years. The proportion of expenditures for educational purposes coming from federal funds has been increasing, but the federal role is still a minor one. Source: U. S. Office of Education, Statistical Summaries of Education for 1935-1936, 1939-1940 and 1943-1944.

assistance, aid to the blind and aid to dependent children. Total costs for these programs have mounted steadily, and the proportion of federal to state and local funds has risen from about 44 per cent in 1939 to 53.5 per cent in fiscal 1946-1947. The absolute and relative rise in federal funds has occurred even though in recent years the states have been strong financially, while the federal government has incurred a tremendous public debt. Federal control over funds expended through state public welfare agencies is concerned with standards of assistance and administration. While the states have sometimes chafed under these controls, they nevertheless have demanded and obtained continuing increase in federal funds (chart 3).

In the case of other social security programs the picture is confusing. Old age and survivors insurance is completely federalized; the states have no part in it. On the other hand, the states administer unemployment compensation, although the original inducement to adopt this program came from the Federal Social Security Act. Unemployment benefits are paid from state trust funds, but the cost of administration is borne by federal grants. In the case of the railroad workers the picture is again a different one. Both railroad retirement and railroad unemployment and disability benefits are federalized; administration of these programs is in the hands of the U. S. Railroad Retirement Board (table 1). Another major program in a somewhat related field—that of pensions and services for

veterans—is also federalized, although some states have their own veteran programs and a few states pay bonuses or pensions to veterans.

HISTORICAL BACKGROUND OF THE PROPOSAL FOR A CABINET DEPARTMENT

Proposals for a cabinet department for health, education and social welfare functions of the federal government antedate many of the now existing functions in these fields. An early proposal was made in the administration of President Harding, but Congress did not take action at that time. Subsequently, President Hoover sponsored a consolidation of certain federal social activities into a major division of the Department of Interior, under the supervision of an assistant secretary. Again Congress failed to act. With the advent of President Roosevelt's administration in 1933, federal relief, health, educational and other welfare expenditures expanded rapidly. However, the pressure of the economic emergency was such as to push the cabinet proposal into abeyance for the time being, while independent agencies were established to carry out welfare programs. The emergency relief and work relief agencies, of which the most important were Federal Emergency Relief Administration, Works Progress Administration, National Youth Administration, Civilian Conservation Corps and Public Works Administration, have now been disbanded.

During the latter part of the thirties there began a process of consolidation of the remaining health, education and welfare agencies, and under the Reorganization Act of 1939 the Federal Security Agency was created. Within the Federal Security Agency were grouped the Office of Education, the Public Health Service, the Social Security Board, the Food and Drug Administration and the Office of Vocational Rehabilitation. Further additions followed the reorganization plan of 1946. The Social Security Board was reconstituted the Social Security Administration; most of the Children's Bureau was taken from the Department of Labor, and the vital statistics functions of the Census Bureau were added to the Federal Security Agency. Table 2 shows the present units, personnel and expenditures by the Federal Security Agency.

PRESENT PROPOSALS FOR A CABINET DEPARTMENT

In his message to Congress accompanying the reorganization plan of 1946, President Truman said:

". . . The size and scope of the Federal Security Agency and the importance of its functions clearly call for departmental status and a permanent place in the President's Cabinet. In number of personnel and volume of expenditures the Agency exceeds several of the existing departments. Much more important, the fundamental character of its functions—education, health, welfare, social insurance—and their significance for the future of the country demand for it the highest level of administrative leadership and a voice in the central councils of the executive branch.

"Accordingly, I shall soon recommend to the Congress that legislation be promptly enacted making the Federal Security Agency an executive department, defining its basic purpose, and authorizing the President to transfer to it such units and activities as come within that definition. . . ."

Subsequently, several bills were introduced in Congress to carry out the President's suggestions. Two alternative Senate Bills, S. 140 (Fulbright-Taft Bill) and S. 712 (Aiken Bill) were the subject of hearings in February and March, 1947, before the Senate Committee on Expenditures in Executive Departments. After some amendment, S. 140 was reported out to the floor favorably by the committee. In its report to the Senate, the committee said it ". . . is of the opinion that under a departmental set-up the increasingly important functions of the various activities now incorporated in the Federal Security Agency can be brought into closer accountability to the President and to the Congress, and promote increased economy and efficiency in their operations. . . ." The bill is now ready for discussion and action by the Senate when Congress reconvenes for the second session.

PROVISIONS OF THE FULBRIGHT-TAFT BILL

The Fulbright-Taft bill, S. 140 (table 3) calls for a federal Department of Health, Education and Security, headed by a Secretary of Health, Education and Security. There are to be

TABLE 1.—*Federal and State Financing of Social Security and Public*

Program	Administration: Federal	Administration: State and Local	Source of Funds: Federal	Source of Funds: State and Local	Expenditures 1946-1947: Total	Expenditures 1946-1947: Per Cent Federal
Public assistance: Old age assistance	Federal Security Agency	51 state welfare agencies plus county and local agencies	General revenue	General revenue	Benefits: $913,290,373 [1]	56.5
Aid to dependent children	Social Security Administration		General revenue	General revenue	Benefits: $25,127,228 [1]	44.5
Aid to the blind	Bureau of Public Assistance		General revenue	General revenue	Benefits: $33,517,246 [1]	44.7
General assistance (public relief)	None		None	General revenue	Benefits: $144,065,000 [1]	None
Old age and survivors insurance	F. S. A., Social Security Administration, Bureau O. A. S. I.	None	Payroll taxes; O. A. S. I. Trust Fund	None	Benefits: $425,382,000 [2] Administration: $40,788,000	100.0
Railroad retirement	Railroad Retirement Board	None	Payroll taxes, Railroad Trust Fund	None	Benefits: $173,101,000 Administration: $4,756,000	100.0
Unemployment compensation, state plans	F. S. A., Social Security Administration, Bureau of Employment Security	51 state unemployment agencies	Payroll taxes	Payroll taxes; 51 unemployment compensation trust funds	Benefits: $817,817,000 [2] Administration: $59,496,100	Adm: 100.0 Benefits none
Railroad unemployment compensation	Railroad Retirement Board	None	Payroll taxes, Railroad Trust Fund	None	Benefits: $16,617,000 [2] Administration: $4,561,000	100.0

1. Administrative costs not yet available. 2. Withdrawn from trust funds.
Source: Social Security Bulletin, September 1947; U. S. Railroad Retirement Board.

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three major divisions of the department, each headed by an under secretary. The Under Secretary for Health is to supervise the Bureau of Health; the Under Secretary for Education, the Bureau of Education, and the Under Secretary for Public Welfare, the Bureau of Public Welfare. The bill gives the department no additional functions or authority, but merely lists functions authorized by prior legislation.

Certain transfers are specifically provided. To the Bureau of Health will go the U. S. Public Health Service, the Food and Drug Administration, Freedmen's Hospital and Saint Elizabeths Hospital. To the Bureau of Education will go the U. S. Office of Education, Howard University, the American Printing House for the Blind and the Columbia Institution for Deaf. To the Bureau of Public Welfare will go the Social Security Administration, which in volume of expenditures is by far the most important of the constituent units of the present Federal Security Agency.

who testified confined their objections to the specific wording of the two Senate bills, S. 140 (Fulbright-Taft Bill) and S. 712 (Aiken Bill), and the only real opposition to this grouping of functions came from the members of the medical profession. Their opposition was related to having health grouped with education and security functions, in the fear that health interests would be subordinated to public welfare and social security. Organized medicine expressed itself in favor of a Department of Health or, failing that, an independent health agency. Other groups, such as consumer protection groups and proponents of child welfare, expressed fears that their interests might not be adequately represented in a new department. However, aside from that of members of the medical profession, no testimony at the hearing expressed real opposition to cabinet status for governmental functions in the fields of health, education and security.

Assistance Programs, Fiscal Year July 1, 1946 to June 30, 1947

Taxes Collected 1946-1947	Beneficiaries June 1947	Trust Fund, as of June 30, 1947	Method of Financing
General tax sources	2,271,097	None	Public assistance payments are made by state and/or local welfare agencies, from state and local funds, with the aid of federal grants. The programs are noncontributory; except in a few states, there are no taxes specifically earmarked for this purpose
General tax sources	1,009,475	None	
General tax sources	79,033	None	
General tax sources	335,000	None	General assistance payments are made by state and local welfare agencies, from state and local funds. There is no federal participation at the present time. The programs are noncontributory; except in a few states, there are no taxes specifically earmarked for this purpose
$1,459,492,000	Primary only: 797,927 Total: 1,832,285 (includes dependents and survivors)	$8,798,015,000	No state participation. Financed by Federal Insurance Contributions Tax, at present 1 per cent of wages up to $3,000 per year on both workers and employers in covered industries, or a total of 2 per cent of taxable payroll
$380,057,000	Primary: 180,484 Total: 231,213 (includes survivors)	$824,858,000	Financed by federal payroll taxes on railroads and employees, on wages up to $3,600 per year. Tax rate on each rose from 3.5 per cent to 5.75 per cent in January 1947, or a total of 11.5 per cent of taxable payroll
State: $1,001,504,000 Federal: $184,823,000	1,006,000 (weekly average)	$7,863,014,000	Financed by payroll taxes on employers only on wages up to $3,000 per year in covered industries. Federal tax is 0.3 per cent of taxable payroll; state taxes now average about 1.5 per cent. Administration costs are paid from federal grants to states; benefits are paid from state trust funds
$141,750,000	34,000 (daily average)	$859,498,000	Financed by federal payroll taxes on railroads of 3 per cent of wages up to $3,600 per year. No experience rating provisions. This tax will also pay the costs of temporary disability compensation starting July 1, 1947. No state participation

The department is given the following functions: (*a*) to promote, foster and encourage the development throughout the nation of services, facilities and activities in the fields of health, education, public welfare and related fields; (*b*) to collect and analyze statistics and make studies, investigations and reports on conditions, problems and needs in those fields in the United States and in other countries, and to disseminate and make available information in those fields; (*c*) to make reports and recommendations with respect to the most effective policies and methods for the promotion of health, education, public welfare and related services, including recommendations with respect to legislation and matters of administrative policy; (*d*) to advise and cooperate with international organizations functioning in those fields, and (*e*) to administer such federal programs, including grants in aid, and such powers, functions and duties in those fields as are assigned to it or provided through this or subsequent legislative enactment.

OPPOSITION TO THE BILL

Little opposition to the idea of a cabinet Department of Health, Education and Security came out at the hearings on bills S. 140 and S. 172. Representatives of special interests

SIGNIFICANCE OF CABINET STATUS

It would appear that while adoption of this bill would actually mean little change at present in activities covered by the three divisions of the department (at operating levels it would probably be confined to a new letterhead on the stationery), potentially it may have great significance. In the immediate future the Secretary of Health, Education and Security would sit in at cabinet sessions and would have direct access to the President. Even now, without cabinet status, the administrator of the Federal Security Agency is in close contact with the President. Oscar Ross Ewing has recently been appointed to this post, and his views have not yet been made public. However, the previous administrator and the President have both repeatedly stated their proposals for furthering the functions and activities of the Federal Security Agency in a variety of ways: nationalizing unemployment compensation and raising benefit levels; liberalizing coverage and benefit provisions of old age and survivors insurance; increasing federal grants for public assistance; extending public health services, and creating a major new function—an extended, comprehensive plan for compulsory federal health insurance.

To date, Congress has been reluctant to adopt these proposals for greatly increasing federal responsibilities and expenditures along such lines largely because of the heavy taxes which would be necessary to pay for them. A cabinet secretary of health, education and security may be more successful, for he would tend to have greater prestige with Congress.

WOULD A CABINET DEPARTMENT BE MORE EFFICIENT?

A cabinet department might be more efficient if it provided for a real consolidation of constituent units, elimination of duplication and overlapping and cutting down personnel requirements. It appears that on the whole the administration of the Federal Security Agency has been effective and efficient. However, the constituent units have functions which are not closely related. As a result, coordination among them has tended to be loose, and the separate branches within the agency have operated much as if they were independent of each other. It is possible that a drive for effective coordination and economy could readily be made under the existing set-up. Cabinet status would not be necessary for this. A cabinet secretary may be more interested in efforts toward further expansion of the functions of his department.

WOULD A CABINET DEPARTMENT BE MORE RESPONSIBLE TO CONGRESS?

Here, again, it is doubtful whether cabinet status per se would count for much. Both administrators of independent agencies and cabinet secretaries must go to Congress for legislative authority and for appropriations, and both have generally asked for constantly increased appropriations and expanding functions. There is no reason to believe that the situation would not be the same with a cabinet Department of Health, Education and Security, but there is some reason to expect that a cabinet secretary, enjoying greater prestige with the President and with Congress, may be more successful. Indeed, a cabinet secretary is primarily a political figure, whereas an independent career official may be first an administrator and only second a politician.

SHOULD A CABINET DEPARTMENT GO BEYOND MAKING RECOMMENDATIONS?

As clearly stated in the bill, one of the functions to be granted the new department is to make reports and recommendations on legislation and matters of administrative policy. Under a

TABLE 2.—*Present Organization and Appropriations of the Federal Security Agency*

Branch or Division	Number of Employees, S.pt. 30, 1947	Appropriations or Other Funds Available, Fiscal Year 1947-1948 (in Thousands): Grants-in-Aid and Anticipated Benefits	Administration, Research, Etc.	Total	Major Functions: Operation or Administration of	Administrative Head
"Health" group						
Public Health Service	16,232	$59,390	$58,458	$117,848	Public health services; grants to state for health services	Surg. Gen.: Thomas Parran Deputy: James A. Crabtree
Freedmen's Hospital	768	.....	2,192	2,192	General hospital	Super.: James L. Hall
St. Elizabeths Hospital	2,448	.....	1,550	1,550	Hospital for mentally ill	Super.: Winfred Overholser
Food and Drug Administration	1,002	.....	4,531	4,531	Regulating of food and drug purity and labeling	Com.: Paul B. Dunbar
Subtotal	20,390	59,390	66,731	126,111		
"Education" group						
Office of Education	403	20,395	1,634	21,999	Compilation of school statistics, grants for vocational education	Com.: John W. Studebaker
American Printing House for the Blind	...	125	.....	125	Education for blind students	
Columbia Institution for Deaf	101	...	200	200	Washington school for deaf	Pres. of Bd.: Percival Hall
Howard University	861	...	4,287	4,287	Higher education for Negroes	Pres. of Bd.: Mordecai Johnson
Subtotal	1,365	20,490	6,181	26,671		
"Security" group						
Bureau of Employees' Compensation	376	10,350	1,316	11,666	Compensation for occupational injury or disease, federal employees	Dir.: William McCauley
Social Security Administration	.....	.....	.....	.....	.....	Com.: Arthur J. Altmeyer
Bureau of Old Age and Survivors Insurance	11,476	522,000 [1]	35,755	557,755	Old age and survivors insurance	Dir.: Oscar C. Pogge
Children's Bureau	255	25,000	1,181	26,181	Child welfare; grants to states for maternal and child health services [4]	Head: Katharine F. Lenroot
Bureau Employment Security		966,512 [2]	948	967,460	Unemployment compensation	Dir.: R. G. Wagenet
Bureau Public Assistance	1,216	625,000 [3]	1,150	626,150	Old age assistance, aid to blind, aid to dependent children	Dir.: James M. Hoey
Other		.....	2,430	2,430	Research, coordination, etc.	
Subtotal, S. S. A.	12,927	2,158,512	41,434	2,179,976		
Subtotal	13,303	2,148,762	42,780	2,191,542		
"Unclassified" group						
Office of Vocational Rehabilitation	131	18,000	550	18,550	Treatment and retraining of handicapped persons	Dir.: Michael J. Shortley
Office of the Administrator	329	850	3,909	4,759	Over-all administration	Admin.: Oscar Ross Ewing Ass't.: Maurice Collins
Subtotal	460	18,850	4,459	2.,319		
Grand total	35,518	2,247,492	120,151	2,367,643		

1. Anticipated benefit payments from O. A. S. I. trust fund.

2. Includes anticipated benefits from state unemployment compensation trust funds of $900,000,000; federal grants to states of $65,612,000 for administration of unemployment compensation, and $300,000 anticipated unemployment benefits to seamen.

3. Federal share only: does not include anticipated state expenditures for old age assistance, aid to blind and aid to dependent children.

4. While the Children's Bureau has important health functions, it is now part of the Social Security Administration and thus included here in the security group.

Source: Federal Security Agency, office of the administrator.

The "security" group of the constituent units of the Federal Security Agency, with about one third of the total personnel, will have control over more than 92 per cent of the total funds available in fiscal 1947-1948. The "health" group, with over half of the personnel, will account for about 5.3 per cent of total anticipated expenditures. "Education" trails a poor third, with less than one twenty-fifth of the personnel and less than 2 per cent of the funds. It would appear that there is some justification for the fear on the part of some persons that educational and health interests in a cabinet Department of Health, Education and Security may be subordinated to "security" interests.

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similar provision of the original Social Security Act, the Social Security Administration has been in the past and is now active in recommending legislation. Recommendations have generally taken the form of proposals for broadening coverage, increasing benefits and raising taxes under present social security programs—and for including compulsory health insurance in social security. The Social Security Board, now the Social Security Administration, has liberally interpreted its function for recommending additional legislation. It is possible that its officials look forward to cabinet status in the hope that their proposals will receive more favorable attention.

SHOULD OTHER AGENCIES BE INCLUDED?

A section of S. 140 delegates to the Bureau of the Budget the task of studying functions now in other agencies and departments of the federal government with a view to possible inclusion in the proposed Department of Health, Education and Security ". . . in the interest of economy and simplicity of administration." Agencies which might thus be considered include the Bureau of Human Nutrition and Home Economics now in the Department of Agriculture, the Railroad Retirement Board, the Federal Public Housing Authority, the Office of Indian Affairs now in the Department of Interior, probation and parole work now in the Department of Justice, educational activities now in the Smithsonian Institution and the Veterans Administration. All these agencies function in fields more or less related to health, education or public welfare, and there may be others. The Bureau of the Budget is directed to submit its recommendations to Congress in a designated period of time. The effect of their inclusion (which, however, would probably be opposed by those who have special interests in these agencies) would be to expand further the functions, personnel and expenditures of the department.

PUBLIC ASSISTANCE AND THE FEDERAL GOVERNMENT

At the present time there is no federal participation in general assistance, or direct public relief, other than for the categorical aid programs (old age assistance, aid to the blind and aid to dependent children). Both total costs and the federal share for these programs have steadily increased, despite high prosperity and employment. There is a movement to obtain regular federal aid for general assistance as well as categorical programs, and it is general assistance which fluctuates most directly with the level of economic activity. If such proposals are adopted, they would greatly increase federal expenditures and administrative scope even under full employment.

IN THE EVENT OF A DEPRESSION

It is to be hoped that the nation will not again face an economic crisis such as that of the thirties, with widespread unemployment and acute distress. Nevertheless, the possibility must be faced. During that period, the federal administration obtained congressional approval for unprecedented welfare measures. A large group of powerful independent agencies were established for direct and work relief, including the Civil Works Administration, the Federal Emergency Relief Administration, the Public Works Administration, Civilian Conservation Corps, National Youth Administration and Works Progress Administration. These agencies accounted for a major share of federal expenditures in the thirties. While some of them continued in existence for several years after the economic emergency had subsided, nevertheless, as temporary agencies, they were eventually disbanded.

With a cabinet Department of Health, Education and Security, the logical place for the expansion of relief measures would be within that department. Functions that in the thirties were assigned to temporary agencies would probably go to the department; indeed, the department would likely have sufficient political strength to play a major part in initiating legislation to this effect. There is danger that a single cabinet department, combining extensive regular functions with a new F.E.R.A., W.P.A., N.Y.A. and C.C.C., might obtain such power and control over public funds as to constitute a real threat to democratic government and freedom of enterprise.

Then, too, incorporation of emergency functions in a permanent department may tend to have the effect of perpetuating such functions long after the reason for their establishment has disappeared. These possibilities may seem remote at present, but they merit careful consideration from both Congress and the public in weighing the cabinet proposal.

TABLE 3.—*Provisions of S. 140*

Introduced by:	Fulbright, Democrat, Arkansas; Taft, Republican, Ohio
Date:	Jan. 10, 1947
Disposition:	Reported with amendment by Aiken, R., Vermont, by Committee on Expenditure in the Executive Departments, on June 6, 1947
Title:	"Health, Education, and Security Department Act of 1947"; A bill to create an executive department of the government to be known as the Department of Health, Education and Security
Administrative heads:	Under direction of the Secretary of Health, Education and Security at $15,000 a year (The secretary is to appoint advisory committees to consult on matters of policies and procedures) Under Secretary for Health at $12,000 a year Under Secretary for Education at $12,000 a year Under Secretary for Public Welfare at $12,000 a year (One of these to act as secretary in case of absence or vacancy in the secretary's office)
Purpose of department:	"To promote the general welfare of the people of the United States by aiding and fostering progress . . . in the fields of health, education, public welfare and related services
Duties of department:	"1. Promote, foster and encourage the development . . . of services, facilities and activities in the fields of health, education, public welfare and related fields "2. Collect and analyze statistics and make studies, investigations and reports on conditions in those fields in the United States and other countries, and disseminate and make available information in those fields "3. Make reports and recommendations with respect to the most effective policies and methods for the promotion of health, education, public welfare and related services, including recommendations with respect to legislation and matters of administrative policy "4. Advise and cooperate with international organizations functioning in those fields "5. Administer such federal programs, including grants-in-aid, and such powers, functions and duties in those fields as are assigned to it or provided through this or subsequent legislative enactment"
Administrative system:	Creates the following bureaus, with designated transfers. Divisions of the department are to be, in order of descending ranking, bureaus, divisions, branches, sections and units Bureau of Health.—U. S. Public Health Service, Food and Drug Administration, Freedmen's Hospital and St. Elizabeths Hospital Bureau of Education.—U. S. Office of Education plus Howard University, American Printing House for the Blind and the Columbia Institution for Deaf Bureau of Public Welfare.—Social Security Administration Transfers existing personnel, equipment, appropriations, etc. of the foregoing agencies. In addition, the secretary is authorized to appoint a general counsel and to create such additional divisions, branches, etc., as he deems necessary
Grants-in-aid:	The secretary is directed to establish uniform standards and procedures relating to fiscal, personnel and other requirements for grants, and standards and procedures to enable state agencies receiving more than one grant to submit a single plan of operation and to be subject to a single fiscal and administrative review of its operation
Reports to Congress:	The secretary is required to prepare a report to Congress at the close of each fiscal year, giving an account of expenditures, describing the work done by the department, and making such recommendations as he deems necessary
Effective date:	Ninety days after date of enactment
Transfers of other agencies:	Director of the Bureau of the Budget is authorized and directed to study activities of other departments and agencies in the federal government and report to Congress on whether any of them should be transferred to the new department in the interest of economy and simplicity of administration

WHAT ABOUT THE FURTHER DEVELOPMENT OF FEDERAL AND STATE RELATIONSHIPS?

Of more immediate interest is the need for a clear definition of the division between federal, state and local responsibility for matters of health, education and public welfare. Expansion of social activities at all levels of government has been piece-

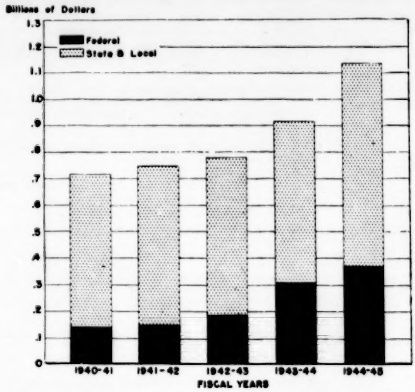

Chart 2.—Public expenditures for health and medical care services. Total public expenditures for health and medical care services increased 58.5 per cent from 1941 to 1945, while the federal share increased 167 per cent. Not included are health services incidental to other functions, such as public assistance, the Army, the Navy and education. Source: Social Security Yearbooks.

meal, in response to specific needs and demands. The line of demarcation between areas of responsibilities grows ever hazier. There are those who believe that these matters are and should be the responsibility only of states, individuals and communities. In contrast, others believe that local groups cannot be relied on to handle them and that the federal government alone should take over the task of providing health and social services. By way of compromise between these two extreme views, the grants-in-aid principle has been the means of extending federal participation (chart 4).

The effect of a cabinet department may be to hasten federal encroachment. The bill would not prevent such a development. Its only safeguard of local and voluntary interests is the

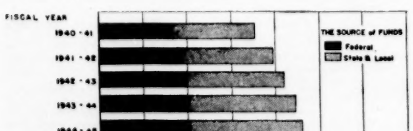

Chart 3.—Total costs for categorical aid programs of public assistance (old age assistance, aid to the blind and aid to dependent children). Total costs for these programs have risen 68 per cent in seven years, while the federal share has nearly doubled. Source: Social Security Administration. Includes benefits and administration. Column marked (1) excludes administrative costs paid from state sources; not yet available.

following sentence in the bill: ". . . Nothing in this Act shall be construed as conferring on any Federal officer or employee the right to exercise any supervision or control over the administration, personnel or operation of any State or local agencies, public or voluntary, in the fields of health, education, public welfare or related services. . . ." This sentence, added by the Senate Committee on Expenditures in Executive Departments, replaced the original wording in the bill as introduced by Senators Fulbright and Taft:

". . . The Department shall promote the general welfare of the people of the United States by aiding and fostering progress throughout the Nation in the fields of health, education, security, and related services contributing to individual, family and community well-being; and these objectives shall be carried out to the fullest possible extent through State and local agencies, public and voluntary, and in such manner as to preserve and protect to the highest possible degree the independence and autonomy of State and local agencies, public and voluntary, in education, health, security and related fields. . . ."

It is apparent that the amended version of the bill weakens the provision on behalf of local and voluntary interests in these fields. The bill does not require federal development or encouragement of local interests. If adopted in its present form, the effect of the bill (depending partly on federal administrative policy) may well make for discouragement of voluntary and local action.

Before action is taken on the cabinet proposal, it would appear that an essential first step would be discussion of the proper relationship between federal and state-local responsibility. This relationship should be clarified, and it is desirable

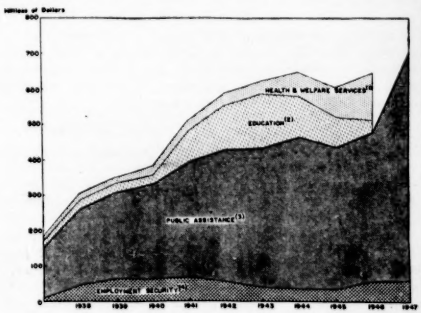

Chart 4.—Federal grants to states for health, education and security purposes by fiscal years ending June 30:

(1) Maternal and child health and welfare services, public health services, venereal disease and tuberculosis control, vocational rehabilitation, state and territorial homes for disabled soldiers and sailors, emergency maternity and infant care, and school-lunch program. 1947 data not yet available.

(2) Education of the blind, agriculture and mechanical arts colleges, marine schools, vocational education, training of war workers and services for farm labor, 1947 data not yet available.

(3) Old age assistance, aid to dependent children and aid to blind.

(4) Unemployment compensation administration; employment services through 1941.

Since 1943, there has been a decline in grants to states for education, due to the curtailment of defense training programs. Grants for employment security purposes have shown some fluctuation, but grants for public assistance and health and welfare services have steadily increased. In the last two years public assistance grants have risen more than 50 per cent, from $421.2 millions in 1946 to $644.1 millions in 1947. Source: Social Security Yearbook, 1945, and Social Security Bulletin, September 1947.

that such clarification should come at a period such as the present when there is no economic crisis bringing pressure on Congress for immediate federal expansion.

In conclusion, it is doubtful whether granting cabinet status to the Federal Security Agency has any real value other than a frankly political one. On the other hand, this proposal, of little apparent significance in the immediate future, may contain implications for the potential growth of the Department of Health, Education and Security of such magnitude as to merit careful consideration. Further study of all possibilities is necessary before Congress acts on S. 140.

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Official Notes

RADIO PROGRAMS

The A.M.A.-N.B.C. radio program, "Doctors Today," which opened Dec. 13, 1947, is scheduled to run for twenty-six consecutive weeks at 3 p. m. each Saturday, Chicago time. The exact number of stations taking the program will be announced when available; the 1947 series "Doctors—Then and Now" was broadcast by approximately one hundred and forty stations coast to coast.

"Doctors Today" is a program based on timeliness and therefore subject to change. The following schedule is tentative. Announcement of changes will be made in THE JOURNAL whenever possible, but there may be times when the program broadcast will not coincide in subject or title with that previously announced.

Whenever possible programs canceled in favor of more timely ones will be broadcast later in the series.

Following is the schedule for programs now contemplated:

January 10, Care of the Chronically Ill.
January 17, Alcoholism.
January 24, Federal Control of Drugs
January 31, Urgent Need for Nurses.
February 7, Health in Rural Schools.

Washington Letter

(From a Special Correspondent)

Jan. 8, 1948.

Insanity Rate Higher in War Years

The U. S. Census Bureau reported that there was an increase in insanity among Americans during the war years, 1940 through 1945, especially among men in the military age bracket. The question was posed whether the "psychologic hazards of military life" drove more men insane or whether the intensive psychiatric scrutiny given men in this age group detected more cases of insanity. The increase in insanity among women paralleled that of men, but it was less in the 20 through 34 age group. The report covered the rise in the rate of first admissions of psychotic persons and it ignored hospital admissions of psychoneurotics and marginal disorders such as alcoholism, mental deficiency or drug addiction. The estimated number of first admissions to hospitals for permanent care of all patients with psychosis increased from 71.7 in each hundred thousand of population in 1940 to 86.8 in 1945, an increase of about 21 per cent. The number of men admitted to hospitals as psychotics was 78.8 per hundred thousand in 1940 as against 96.4 in 1945. Admissions more than doubled among men aged 20 to 24, rose 78 per cent among those aged 25 to 29 and rose 36 per cent among those aged 30 to 34.

Hawley Reports Veterans Administration May Lose Fourteen Hundred Doctors

Major Gen. Paul R. Hawley, former veterans' administrator, reported just prior to his retirement that the agency faces the loss of more than fourteen hundred physicians next spring, when terms of young officers trained in the wartime Army specialized training and V-12 programs expire. Many of the officers were assigned to isolated hospitals for which it was difficult to obtain civilian personnel, and many of them have expressed their intention to leave the agency on completion of the two year terms. The agency employs about sixty-seven hundred physicians in its hundred and twenty-six hospitals serving 118,000 patients.

Order to Curb Venereal Disease

Army Secretary Kenneth C. Royall has issued orders for a new drive to combat venereal disease among enlisted men. Officers and men who become infected are prohibited from leaving camp for thirty or even ninety days and are denied the right to visit their homes for at least thirty days after being cured; promotions will be withheld for men with repeated infections; cooperation with civilian authorities in combating prostitution near military establishments and in sponsoring athletic and recreation programs will be encouraged.

Office of Scientific Research and Development Abolished

President Truman signed the executive order abolishing the wartime Office of Scientific Research and Development, the duties of which were absorbed by the unified armed services. Dr. Vannevar Bush, former head of the Office of Scientific Research and Development, is chairman of the new research and development board set up within the national military establishment under the unification act.

Federal Aid for Needy College Students Urged by Presidential Commission

The President's Commission on Higher Education advocates that $135,000,000 be provided by the federal government to aid needy college students in 1948-1949. The expenditure was proposed as a starting point for federal assistance to equalize educational opportunity for deserving students throughout the nation.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Admission of Mental Patients at Saint Elizabeths Hospital

Companion bills have been introduced to provide for the voluntary admission and treatment of mental patients at Saint Elizabeths Hospital, S. 1810, introduced, by request, by Senator Taft, Ohio, and H. R. 4552, introduced by Representative Buck, New York. The Superintendent of the Hospital would be authorized, with the approval of the Federal Security Administrator, to prescribe such regulations as he shall deem necessary to carry out the provisions of the legislation.

National Board of Medical Examiners

A pending bill, H. R. 4636, introduced by Representative Miller, Nebraska, proposes to amend the healing arts practice act of the District of Columbia so as to authorize the issuance of licenses, without examination, to applicants who hold certificates issued by the National Board of Medical Examiners.

Importation of X-Ray Film

A bill introduced by Representative Andresen, Minnesota, proposes to amend paragraph 1629 of the Tariff Act of 1930 so as to provide for the free importation of exposed x-ray film. The purpose of this legislation is apparently to permit patients who have received treatment abroad to bring in to this country free of any tariff roentgenograms which may have been taken in connection with such treatment.

Hospital Construction

Delegate Bartlett, Alaska, proposes by H. R. 4816 to amend the federal hospital survey and construction act so as to provide the minimum allotment of $250,000 to each state for the construction of hospitals.

A bill introduced by Representative Fallon, Maryland, provides that the funds heretofore appropriated for the construction of a Veterans' Administration tuberculosis hospital in Baltimore shall be used for the construction in that city of a general medical and surgical hospital.

Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 9-10. Dr. Donald G. Anderson, 535 North Dearborn St., Chicago 10, Secretary.

National Conference on Rural Health, Chicago, Palmer House, Feb. 6-7. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

American Academy of Orthopaedic Surgeons, Chicago, Palmer House, Jan. 24-29. Dr. Harold B. Boyd, 869 Madison Ave., Memphis, Tenn., Secretary.

American Society for Surgery of the Hand, Chicago, Jan. 23-24. Dr. Joseph H. Boyes, 1401 S. Hope St., Los Angeles 15, Secretary.

Southeastern Allergy Association, Richmond, Va., Jefferson Hotel, Jan. 17-18. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

GOVERNMENT SERVICES

ARMY

IMPROVEMENTS IN ADVANCED TRAINING FOR MEDICAL OFFICERS

The Surgeon General announced December 20 a number of changes in the Medical Department graduate education program for the coming year, based on nine months' operation of the program and surveys made by civilian medical experts. The innovations, effective immediately, are designed to maintain the quality of patient care and to elevate the caliber of training at Army general hospitals. The major changes are as follows:

Graduate training in psychiatry is being strengthened and concentrated in three general hospitals—Letterman (San Francisco), Fitzsimons (Denver) and Walter Reed (Washington, D. C.). This plan will afford each resident more individual instruction. Many qualified civilian consultants will be added to the attending staffs of the hospitals which are engaged in teaching. The administrative responsibilities of qualified teachers will be lessened by the transfer of routine paper work to administrative assistants assigned from the Medical Service Corps. Qualified instructor personnel will be kept on duty in their present assignments for as long as possible. When it becomes necessary to move them, they will be placed in locations where they will be able to teach.

Special instruction in the best methods of medical education is being provided for key military instructor personnel by means of short courses at selected civilian medical institutions. The number of conferences at which attendance by residents and interns is required is being reduced. Where possible, these will be held at times that will not interfere with bedside teaching. Likewise, the administrative duties of student officers are being reduced to the bare minimum consistent with excellent care of patients under their supervision. More adequate means of resident-intern selection and evaluation of progress are being placed in operation. Personal interviews will receive special emphasis. The present obstacles in the organization of interns and residents into the accepted pyramidal system are being overcome, so that the student officers may be given increased responsibility in care of patients, teaching and the supervision of others as they progress from one year of training to the next.

The Surgeon General pointed out that the improvements are a part of a continuing effort to place Army teaching hospitals on an equal plane with the best civilian teaching hospitals. He reported that the internists, surgeons and psychiatrists who surveyed nine Army general hospitals found that professional training compares favorably, for the most part, with the residency training given at civilian teaching centers with which they are familiar.

At present two hundred and four officers of the Regular Army Medical Corps are participating in the postgraduate instruction program as residents. The objective of each is certification as a diplomate by one of the specialty boards. In addition, fifty positions were made available on January 1 to applicants for the Regular Army who are now in the continental United States, and fifty more will be offered to applicants who are overseas effective July 1. The Surgeon General will furnish further information to interested doctors.

Of the one hundred and six applicants who have been approved thus far for internships beginning July 1, thirteen had a scholastic standing among the first ten of their class. Thirty others stood in the first third of the respective classes, and fifty-eight were in the middle third.

The hundreds of Army physicians who will receive internship and residency training this year and next, with some of the nation's leading specialists as well as war-seasoned military medical personnel as their instructors, constitute a group separate and distinct from others receiving special courses in civilian hospitals and schools.

GENERALS NOMINATED FOR PROMOTION

The Army's First Selection Board under the new Officer Personnel Act has submitted to President Truman the names of seventy-six officers for promotion to the grade of permanent major general and ninety-two for promotion to permanent brigadier general in the Regular Army. The President has approved the list and sent it to the Senate for confirmation. In the medical corps the following five were recommended for confirmation to major general: George C. Beach Jr., Raymond W. Bliss, Malcolm C. Grow, Albert W. Kenner and John M. Willis; the five recommended for permanent promotion to brigadier general are James A. Bethea, Guy B. Denit, Joseph I. Martin, Edward A. Noyes and Omar H. Quade.

AFFILIATED UNITS OF THE MEDICAL DEPARTMENT

Eleven medical schools and hospitals to date have signed agreements with the Department of the Army to sponsor affiliated units of the Medical Department, thus becoming integral members of the organized Reserve. In making the announcement Major Gen. Raymond W. Bliss, the Surgeon General, expressed gratification with the response, adding that he confidently expects many more institutions to join in coming months.

Medical Schools of the Universities of Texas, Illinois, Wisconsin, Marquette, Ohio State, Duke and Baylor have completed negotiations to sponsor affiliated units, as have the following hospitals: Mount Sinai (New York), Cook County (Chicago), Rochester General (Rochester, N. Y.) and Boston City Hospital (Mass.).

The affiliated unit inaugurated by the Army in World War I proved to be an invaluable asset in World War II, when some five hundred affiliated units—not only medical but signal, railroad, engineering and numerous other types—saw service in all theaters of operations.

MEETING OF MEDICAL OFFICERS IN KOREA

At the regular monthly meeting of U. S. Army medical officers stationed in Korea at the 34th General Hospital, Dec. 17, 1947, among those present were Col. G. N. Schuhmann, M. C., U. S. A., and Col. R. E. Blount, M. C., U. S. A, who were visiting Korea as consultants in preventive medicine and medicine, respectively. The following papers were presented: "The Action of Anesthetics on Respiration" by Capt. Clara A. Vezina, A. N. C., discussed by Lieut. Kay Shaffer, A. N. C.; "Functional Illness" by Capt. Raymond C. Perkins, M. C., discussed by Colonel Blount and Capt. Irving Schulman, and "Preparation of Hospital Records" by Capt. Charles A. Cubbler, S. C. Dr. Philip Jaisohn, a Korean patriot who addressed the November meeting, spoke on "Adventures in Recent Korean History." Dr. Jaisohn is 81 years of age; he is now acting as special advisor to Lieut. Gen. John R. Hodge, commanding general, U. S. Army Forces in Korea. There were also ward rounds and departmental conferences. The hospital registrars in Korea were especially invited to attend this meeting. The chairman was Lieut. Col. John J. Marren, commandant of the 34th General Hospital. The business meeting was in charge of Col. Charles P. Ward, M. C., surgeon, 24th Corps.

PERSONAL

Dr. Henry M. Thomas, colonel, M. C., reserves, of Baltimore, has been placed on active duty for a period of five weeks, as medical adviser to Major Gen. Willard S. Paul, director of Personnel and Administration (G-1) Department of the Army.

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NAVY

GROUP TO STUDY CHOLERA EPIDEMIC IN SYRIA

The Medical Department of the Navy is sending four specialists to Syria to study the cholera epidemic in Damascus and other parts of Syria. Emphasis will be placed on preventive and epidemic control measures. The party will consist of Lieuts. (jg) Richard H. Weaver (MC), U. S. N. R., of Kalamazoo, Mich., and Moulton K. Johnson (MC), U. S. N. R., of Washington, D. C.; Chief Pharmacist Mate James D. Gillmore, U. S. N., of Mount Vernon, Wash., and Pharmacist Mate, first class, Charles F. Robinson, U. S. N., of Corpus Christi, Texas. The group is now on duty at Naval Medical Research Unit 3 in Cairo, Egypt. Each member of the Syrian party is an expert in the prevention and control of cholera, and each participated in the recent naval medical program which assisted the Egyptian government to curb the cholera epidemic in Egypt.

MEETING OF HONORARY CONSULTANTS

The Honorary Civilian Consultants to the Medical Department of the Navy met December 5 in Washington, D. C. The consultants, who are appointed by the Secretary of the Navy, act as an advisory board to assist in formulating policies for the Bureau of Medicine and Surgery. The welcoming address was made by the Under Secretary of the Navy, the Honorable W. John Kenney. The Surgeon General, Rear Admiral Clifford A. Swanson (MC), opened the meeting with a discussion of the problems facing the Medical Department for the coming year and was followed by Rear Admiral H. Lamont Pugh (MC), Deputy Surgeon General, who spoke on the Bureau's organization. The consultants were: Dr. Edward L. Bortz, President, American Medical Association, Philadelphia; Dr. Roscoe L. Sensenich, President-Elect, American Medical Association, South Bend, Ind.; Dr. Joseph L. Appleton, Philadelphia; Dr. Richard R. Cattell, Boston; Dr. Robert P. Fischelis, Washington, D. C.; Dr. Evarts A. Graham, St. Louis; Dr. Frank H. Lahey, Boston; Dr. Oswald S. Lowsley, New York; Rev. Paul McNally, Washington, D. C.; Dr. Clyde E. Minges, Rocky Mountain, N. C.; Dr. James Edgar Paullin, Atlanta, Ga.; Dr. Charles Sheard, Rochester, Minn.; Dr. W. Calhoun Stirling, Washington, D. C.; Dr. Edward A. Strecker, Philadelphia, and Dr. Meyer Wiener, Coronado, Calif.

APPOINTMENT OF COMMISSIONED OFFICERS IN THE REGULAR NAVY

The Army-Navy-Public Health Service Medical Officer Procurement Act of 1947 makes it possible now for civilian doctors to become commissioned officers in the regular Navy, provided they meet the professional and physical qualifications. This law is unique in that it does away, for the first time, with the age limitation of 32 years and permits doctors in civilian practice to enter the Navy and be commissioned with the rank up to and including captain. The law considers all strata of the medical profession, interns, residents, reserves, former medical officers who have resigned and presently practicing physicians.

To make application a physician must be a citizen of the United States, a graduate from a class A medical school and must have served at least one year's internship in an approved hospital. Candidates will then be judged on a number of qualifications such as being a member of a specialty board, teaching connections, the number of years of professional or scientific practice, hospital or laboratory connections and a statement of military service.

The allocation of rank to successful candidates will depend on their academic age, professional standing and experience in the medical field. Successful candidates will then be integrated in line with medical officers of the regular Navy and assigned running mates accordingly. This means that they will be eligible for promotion along with their fellow officers of equal rank.

This law offers an opportunity for civilian doctors to make a career in the regular Navy and to enjoy its professional advantages as well as its retirement benefits. Doctors interested in such a career should write to the Bureau of Naval Personnel, via the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

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PUBLIC HEALTH SERVICE

GRANTS FOR TRAINING AND RESEARCH IN PSYCHIATRY AND PSYCHOLOGY

Applications for training and research grants in psychiatry, clinical psychology, psychiatric social work and psychiatric nursing in connection with the program of the U. S. Public Health Service authorized under the Mental Health Act for the fiscal year beginning July 1, 1948 should be received not later than January 15. Final action will be taken on these applications at the next meeting of the National Advisory Mental Health Council in Washington, D. C., May 14-15. Applications for training grants should be sent to the Training and Standards Section and applications for research grants to Research Projects Director, Mental Hygiene Division, U. S. Public Health Service, Washington, D. C.

GRADUATE INSTITUTE IN KENTUCKY ON PSYCHOSOMATIC MEDICINE

The Mental Hygiene Division of the U. S. Public Health Service, in cooperation with the Kentucky State Medical Association, Kentucky Psychiatric Association and Kentucky Department of Health, is holding a postgraduate institute in psychosomatic medicine and mental hygiene at Lexington, Ky., February 3 to 6. Physicians in Kentucky and adjoining states are invited. There is no registration fee. The speakers will include authorities from various states. Among the presentations will be a symposium on drug addiction and another on infant and child behavior, papers on diagnosis and care of epilepsy, psychologic aspects of rheumatoid arthritis, psychic factors in cardiovascular diseases, and the court psychiatrist's view of crimes. On Friday at a joint meeting with the Kentucky Psychiatric Association there will be papers on early schizophrenia and schizoid personality, and psychotherapy for practitioners.

The U. S. Public Health Service is using funds from the appropriation provided by the mental health program for the institute, and if it is well received by physicians similar institutes will be held elsewhere. Those desiring to attend should write direct to the hotels for reservations, mentioning the institute. Blocks of rooms have been reserved in the Lafayette and Phoenix hotels; other hotels in Lexington are the Drake and the Kentuckian.

RECLASSIFY OCCUPATIONAL THERAPISTS

Professional standards for all occupational therapists in the U. S. Public Health Service have been authorized, according to federal security administrator Oscar F. Ewing. Occupational therapists in hospitals operated by the service will be reclassified from subprofessional to professional grades P 1, P 2 or P 3, if they are graduates of approved schools of occupational therapy, or have experience giving them comparable qualifications, and are performing professional occupational therapy.

Unlike the physical therapist category, which also was recently converted to professional status, the subprofessional status for occupational therapists will not be eliminated. Occupational therapy aides still will be needed in the subprofessional grades. Qualified occupational therapists of the U. S. Public Health Service will not be converted from subprofessional to professional status immediately. Individual job descriptions must first be prepared by the incumbents and reviewed by the Classification Section in order to determine the appropriate professional grade.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

Dr. Houssay Delivers Hitchcock Lectures. — Dr. Bernardo A. Houssay of Buenos Aires delivered the Hitchcock Lectures at the University of California, Berkeley, beginning January 8. The lectures, presented periodically under the Hitchcock Foundation, are open to the public. In his lectures Dr. Houssay, who is director of the Institute of Biology and Experimental Medicine in Buenos Aires, partially covered the work for which he, as co-winner, was awarded the Nobel Prize in Medicine in 1947.

Disease Prevention Week in Los Angeles.—The fourth observance of Disease Prevention Week is set for February 15-22 in Los Angeles. The Community Health Association of Los Angeles will conduct the activity in cooperation with the city and county health departments, the county medical association and its Women's Auxiliary, and numerous social and welfare agencies. The public will be invited to sessions that will run all day Wednesday, February 18, in the Biltmore Hotel, Los Angeles. Health exhibits will be displayed in the morning, a luncheon with distinguished speakers will be given at noon, and papers by health authorities will be delivered during the remainder of the day.

Society News.—Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, will address the regular monthly meeting of the Alameda County Medical Association January 15 in the Scottish Rite Temple in Oakland at 8:15 p.m. on "The Present Status of Medical Legislation." The meeting is open to the members of the Bay area medical associations. Dr. Fishbein will also address the Oakland Rotary Club at its noontime meeting January 15 on "Innovations and Scientific Progress in Medicine."——The Los Angeles Society of Allergy, a section of the Los Angeles County Medical Association, has elected the following officers for 1948: Drs. Willard S. Small, Pasadena, president, and Frank G. Crandall Jr., Los Angeles, secretary-treasurer.——The Trudeau Society of Los Angeles at its meeting December 23 elected Dr. Joseph L. Robinson president and Dr. Arthur E. T. Rogers, secretary-treasurer.——The Los Angeles County Medical Association on Dec. 4, 1947 elected Dr. William H. Leake president, and Dr. Richard O. Bullis, secretary-treasurer. They took office January 1.

Dr. Stanley to Head Laboratory for Virus Research.—Wendell M. Stanley, Ph.D., of the Rockefeller Institute for Medical Research, Princeton, N. J., has been appointed to establish and direct a new laboratory of virus research at the University of California, Berkeley-San Francisco. Dr. Stanley will come to Berkeley in July. He will not only direct biochemical research on the Berkeley campus and at the medical school in San Francisco but also cooperate closely with the state program of the College of Agriculture in the same field. Dr. Stanley received his Ph.D. degree from the University of Illinois in 1927. He was a National Research Fellow in Munich, Germany, 1930-1931, and has been with the Rockefeller Institute for Medical Research since 1931 and a member since 1940. He was the Hitchcock professor at the University of California in 1941. In 1946 Dr. Stanley and John H. Northrop, Ph.D., were awarded one half of the Nobel Prize in Chemistry for their research on virus proteins (THE JOURNAL, Jan. 18, 1947, p. 191). Dr. Stanley also received the American Association for the Advancement of Science Prize in 1936, the Isaac Adler Prize by the Medical School of Harvard in 1938 and the Rosenberger Medal by the University of Chicago in 1938.

GEORGIA

Postgraduate Assembly in Atlanta.—The Fulton County Medical Society is sponsoring the Atlanta Postgraduate Medical Assembly at the Academy of Medicine, Atlanta, January 28-30. The speakers will be Drs. Lester Dragstedt, Chicago; Chester S. Keefer, Boston; Andrew C. Ivy, Chicago; Helen B. Taussig, Baltimore; Julius Lempert, New York; Philip S. Hench, Rochester, Minn.; Emmerich von Haam, Columbus, Ohio; Ralph M. Tovell, Hartford, Conn.; Robert Elman, St. Louis; Tom D. Spies, Birmingham, Ala.; Merrill C. Sosman, Boston; Rufus F. Payne, Rome, and Robert B. Greenblatt, Augusta.

ILLINOIS

Personal. — Dr. Harry D. Nesmith of Salem has been appointed as surgeon for the surrounding area for the Baltimore and Ohio Railway, succeeding Dr. Harry A. Cunningham, who resigned after holding the position about thirty years.

Dr. Cheney Retires from Armour and Company.—After thirty-two years' service Dr. Volney S. Cheney, Chicago, retired Oct. 4, 1947 as medical director for Armour and Company and has been succeeded by Dr. Joseph A. Hubata, Chicago. Dr. Cheney, a graduate of Northwestern University Medical School, 1902, was surgeon for the company from 1916 to 1920, when he became medical director. He has retired and moved to Las Vegas, N. Mex. Dr. Hubata before his appointment served for nine years on the medical staff of the West Pullman Works of the International Harvester Company. He is a graduate of the University of Illinois School of Medicine, 1933.

County Society Honors Veteran Member.—Dr. John M. Palmer, Waukegan, was guest of honor at a recent testimonial dinner in Waukegan, sponsored by the Lake County Medical Society. The occasion marked the retirement of Dr. Palmer, who has spent his entire medical career of forty-six years in Lake County. Among the speakers was Dr. John B. Youmans, dean of the University of Illinois Medical School, Chicago, from which Dr. Palmer graduated in 1901. Dr. Palmer served in the Army medical corps in World War I and located in Waukegan when he returned to civilian life. He is a staff member of Victory Memorial and St. Therese hospitals in Waukegan.

Chicago

The First Holmes Lecture.—At a joint meeting of the Institute of Medicine, the Chicago Ophthalmological Society and the Society of Medical History of Chicago at the Palmer House, January 30, Dr. Edward V. L. Brown, Rush clinical professor emeritus of ophthalmology, University of Illinois College of Medicine, will deliver the first lecture under the Rudolph Wieser Holmes and Maria Baxter Holmes Fund. His subject will be "Edward L. Holmes: Pioneer Chicago Eye Doctor."

The Chicago Industrial Health Plan. — An educational program to raise the standards of industrial health and medicine among 1,500,000 workers in Cook County was launched January 1. The Chicago Industrial Health Plan is supported by community groups, health agencies, major labor unions, management groups and welfare associations. Mr. Lester M. Selig, president of the General American Transportation Company, is general chairman; Dr. Frederick W. Slobe, chairman of the Chicago Medical Society's committee on industrial medicine, is chairman of the executive committee, and Alexander Ropchan, executive secretary, health division, Council of Social Agencies, is secretary. Labor organizations are to name a co-chairman. A full time executive director, Percy Shostac, New York, who directed a similar program for Brooklyn, has been appointed. The plan is financed by the state, the Red Cross, the Tuberculosis Institute and the American Cancer Society. It is said that the program will endeavor to carry out recommendations made by the U. S. Public Health Service in its Chicago-Cook County Health Survey. It is hoped that industries will contribute to the educational program.

INDIANA

Hygeia Sent to Legislators.—The House of Delegates of the Indiana State Medical Association has presented members of the Indiana General Assembly with a year's subscription to *Hygeia, the Health Magazine*, published by the American Medical Association.

State Society to Award Keys.—The council of the Indiana State Medical Association has voted to present gold keys to the three seniors of the 1948 graduating class of the Indiana University School of Medicine, Bloomington-Indianapolis, who make the highest grades. The scholarship awards will be presented at commencement exercises next June.

Congressman Harness to Address Secretaries' Conference.—Congressman Forest A. Harness of Kokomo, representing the Fifth Indiana District, will be principal speaker at the annual Secretaries' Conference of the state medical association in Indianapolis on February 15. Head of a house committee investigating lobbying activities of federal employees, he will reveal strategy of the employees who are trying to influence Congress to pass legislation for socialized medicine. Other speakers will be Dr. Elmer L. Henderson of Louisville, Ky., chairman of the American Medical Association Board of Trustees, and Dr. Richard L. Meiling of Columbus, Ohio, secretary of the American Medical Association Council on National Emergency Medical Service. Dr. Albert M. Mitchell, Terre Haute, chairman of the conference committee, will preside.

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LOUISIANA

Society News.—The Rapides Parish Medical Society will celebrate founders' day January 10 at the Bentley Hotel, Alexandria, with scientific papers beginning at 10 a. m., luncheon at 12:15 p. m. and an afternoon session ending at 4:30. Specialists and teachers on the staffs of Louisiana State University and Tulane medical faculties will address the group. In the evening following the annual banquet there will be an address by a guest speaker.

Matas Lectureship Established.—The Beta Iota Chapter (Tulane) of Nu Sigma Nu Medical Fraternity is inaugurating an annual lectureship in honor of its most famous member, Dr. Rudolph Matas, professor emeritus of surgery at Tulane University of Louisiana School of Medicine, New Orleans. The first lecture will be held on January 28 at 8 p.m. in the Hutchinson Memorial Auditorium of the Tulane Medical School. Dr. Alfred Blalock, professor of surgery at Johns Hopkins Medical School, Baltimore, the inaugural speaker, will lecture on "Surgical Treatment of Congenital Cardiovascular Defects." All members of the medical profession are cordially invited.

MICHIGAN

Hospital Staff Honors Dr. Wilson.—The medical and surgical staff of St. Mary's Hospital, Detroit, gave a testimonial dinner Dec. 3, 1947, for Dr. Walter J. Wilson at the Detroit Athletic Club in honor of his fifty years of practice. He was presented a plaque recording the history of his career. Dr. Wilson, a graduate of the Detroit College of Medicine, 1897, is a past president of the hospital's medical staff and a member of its executive staff.

NEW YORK

Nassau County Postgraduate Instruction.—Postgraduate instruction arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health for the Nassau County Medical Society will be given Tuesday afternoons at 4 o'clock in the Nassau Hospital auditorium, Mineola, as follows:

January 20, Dr. Lewis D. Stevenson, New York, Clinical Aspects of Encephalitis and Poliomyelitis.
January 27, Dr. Harry Most, New York, Tropical Disease, Civilian Implications of Military Experience.
February 3, Dr. Edward F. Hartung, New York, Diagnosis and Treatment of Low Back Pain from the General Practitioner's Point of View.
February 10, Dr. E. Charles Kunkle, New York, Headache Mechanisms.

Training Center in the Field of Atomic Energy.—According to the *Army and Navy Journal*, the U. S. Atomic Energy Commission has approved an expenditure of $615,000 to build and equip a six story training and research center on the campus of the University of Rochester. This project was recommended by the commission's Advisory Committee on Biology and Medicine to provide facilities for training medical personnel to meet problems in the field of atomic energy. Under the program physicians will receive graduate training in the use of radioactive isotopes for tracer studies and therapy and in the treatment of radiation sickness; they will be instructed in the pharmacology and toxicology of radioactive materials, the design of radioactive chemical laboratories, principles of shielding, methods of decontamination and the disposal of radioactive waste materials.

New York City

Lectures for Laymen.—The New York Academy, continuing its series of Lectures to the Laity, will present the following program in 1948 at the Academy at 8:30 p.m.:

January 22, Dr. Edward J. Stieglitz, Washington, D. C., On Being Old Too Young.
February 4, Dr. Cornelius P. Rhoads, New York, Perspectives in Cancer Research.
February 26, Dr. William C. Menninger, Topeka, Kan., Psychiatry for Everyday Needs, the George R. Siedenburg Memorial Lecture.
March 11, James B. Conant, Ph.D., president, Harvard University, Cambridge, Mass., The Interrelation of Pure and Applied Science in the Field of Medicine.

Friday Afternoon Lectures.—The January and February program of the New York Academy of Medicine's Friday Afternoon Lectures, given at the Academy at 4:30 and open to members of the medical profession and medical students, is as follows:

January 16, Dr. Richard H. Freyberg, Diagnosis and Treatment of Arthritis.
January 23, Dr. Murray H. Bass, Recent Advances in Knowledge of Contagious Diseases of Childhood.
January 30, Dr. Paul Reznikoff, Diagnosis and Treatment of Anemia.
February 6, Dr. Thomas A. C. Rennie, Use and Abuse of Psychotherapy.
February 13, Dr. George M. Lewis, What's New in Dermatology?
February 27, Dr. Carl A. L. Binger, Management of the Emotional Side of Heart Disease.

Experiment in Cardiac Rehabilitation.—The Altro Work Shops, Inc., established thirty-two years ago under the direction of Mr. Edward Hochhauser and his associate Miss Celia Hentell for the rehabilitation of the tuberculous, has undertaken a two year experiment in the field of cardiac rehabilitation of the tuberculous. The facilities of Altro have been offered only to the quiescent or arrested tuberculous patient, for whom it helps to bridge the gap between hospital care and complete social integration. Case histories, including medical, industrial and social work data, together with other factors in the program will be evaluated at the end of the two year experimental period to determine the future content of the program. Minimum admission requirements have been set up. For the initial stage of the program only 20 patients will be admitted to facilitate the study of their progress. Inquiries and applications should be addressed, with the medical abstracts, to Altro Work Shops, Inc., 71 West Forty-Seventh Street, New York.

OHIO

University Establishes Eye Laboratory.—The ophthalmology department of the University of Cincinnati College of Medicine is establishing an eye laboratory under the direction of Dr. Donald J. Lyle, professor and head of the department. The work of the laboratory currently is concerned with the examination of eyes for diagnosis and the preparation of specimens for collection and study. Facilities and services of the laboratory will be available to physicians in Ohio, Indiana and Kentucky. The laboratory has taken over temporary quarters in Pavilion A of the Cincinnati General Hospital and is awaiting assignment to permanent quarters there. The first gift to support the laboratory has been made by the Eastern Hills Lions Club.

PENNSYLVANIA

Typhoid Following Wedding Reception.—Fifteen persons among seventy-six who attended a wedding reception near Lititz in Lancaster County on Thanksgiving Day became ill with typhoid, according to the Associated Press. All doctors in the county have been notified of the outbreak.

Seibert Memorial Award.—Dr. Charles W. Smith, Harrisburg, received the Seibert Memorial Award, having been an adjudged member of the Harrisburg Academy of Medicine under 45 years of age, who has done the most to advance medicine in the last two years. Dr. Smith, a former editor of the *Academician*, official publication of the Academy, is chairman of the committee on graduate education of the Medical Society of the State of Pennsylvania, which this year is conducting a graduate education institute in six centers throughout the state. Presentation of $500 for postgraduate medical study, made possible by a trust fund created in memory of Dr. William H. Seibert, was made at a dinner meeting in the Penn-Harris Hotel, Harrisburg, at the close of the academy's sixteenth annual postgraduate assembly.

Pittsburgh

Huggins Memorial Lecture.—The second annual R. R. Huggins Memorial Lecture of the University of Pittsburgh School of Medicine will be given at 8:30 Friday evening, January 16, at the Mellon Institute Auditorium. The guest lecturer will be Dr. Joseph G. Hamilton of the University of California's Radiation Laboratory, speaking on "Application of Radioactive Substances to Clinical Medicine." The lecture is sponsored by the Phi Delta Epsilon Fraternity, Nu Chapter, and all interested are invited to attend.

TEXAS

Memorial Physiology Professorship.—Through contributions to Baylor University College of Medicine Alumni-Faculty Foundation and by faculty members and other friends, an endowment is being established for a professorship of physiology as a memorial to Dr. Benjamin F. Hambleton, a member of the faculty for twenty-seven years. The professorship will become effective at the beginning of the academic year 1948-1949. Dr. Hambleton was graduated from Ohio Wesleyan University Medical Department, Cleveland, and joined the department of physiology, where he served from 1901 to 1910. He was professor of physiology and pharmacology at Vanderbilt University from 1910 to 1919 and came to Baylor University College of Medicine, Dallas, in 1920 as professor of pharmacology and biochemistry. In 1930 he was appointed professor of physiology and pharmacology, continuing active until his sudden death Dec. 9, 1947, at the age of 75.

GENERAL

Meeting of Spanish Speaking Physicians.—The International Spanish Speaking Association of Physicians, Dentists and Pharmacists, Inc., will meet at the Waldorf-Astoria Hotel, New York, January 23, under the presidency of Dr. Jacob M. Gershberg, New York. Included on the program is a symposium on blood from the points of view of geriatrics, race, life, diseases and crime.

Southeastern Allergy Association.—The third annual meeting of the Southeastern Allergy Association will be held January 17-18 at the Jefferson Hotel, Richmond, Va., under the presidency of Dr. J. Warrick Thomas of Richmond. The program for Saturday includes panel discussions of nose and throat allergies, atopic dermatitis, the effectiveness of influenzal and rickettsial vaccines, and sudden death during skin testing. Guest speakers will be Dr. Karl D. Figley, Detroit, president, American Academy of Allergy, on "Some Unanswered Questions in Clinical Allergy" and Dr. Hal M. Davison, Atlanta, Ga., president, American College of Allergists, on "Allergy and Nutrition." Sunday's program includes a panel discussion and papers on periarteritis nodosa, sensitivity to alcoholic beverages and ascaris asthma.

National Conference on Medical Service.—A National Conference on Medical Service will be held at the Palmer House, Chicago, February 8 beginning at 9 a.m. under the presidency of Dr. Creighton Barker, New Haven, Conn. Subjects under discussion include two points of view on "The Practice of Medicine in Hospitals, Health Departments and Medical Schools," "Medical Public Relations Begin in the Doctor's Office," and "The Nursing Problem in America" in its educational, service and economic aspects. The luncheon speaker will be Robert Hutchins, chancellor, University of Chicago, speaking on "Are Medical Educational Requirements Too High—Should We Have More Doctors?" On the afternoon program are two panel discussions, one on General Practice and another on Specialty Boards.

Gastroenterologic Contest and Award.—The National Gastroenterological Association announces its Annual Cash Prize Awards Contest for 1948 for the best unpublished contribution to gastroenterology. Contestants residing in the United States must be members of the American Medical Association, and those in foreign countries must be members of a similar organization in their own country. The winner will be selected by a board of impartial judges, and the award of $100 and a Certificate of Merit will be made at the annual banquet of the National Gastroenterological Association in June, 1948. The association reserves the exclusive rights to publish the winning contribution and those receiving certificates of merit in its official publication. Entries should be limited to 5,000 words, typewritten in English and submitted in five copies. They must be received not later than April 1, 1948 by the National Gastroenterological Association, 1819 Broadway, New York 23.

Research Fellowships in Medicine.—The American College of Physicians has awarded six Research Fellowships in Medicine for the year beginning July 1948 with stipends ranging from $2,200 to $3,200. Recipients and their fields of research are: Drs. Charles G. Campbell, Montreal, Canada, for studies of the basic physiology of certain cardiovascular problems, at McGill University Faculty of Medicine, Montreal; Frank H. Gardner, Boston, the mechanism and clinical application of the osmotic fragility test, at Thorndike Memorial Laboratory; Samuel P. Martin, Durham, N. C., bacterial metabolism, in the Rockefeller Institute for Medical Research, New York; Peritz Scheinberg, Miami, Fla., cerebral circulation and peripheral vascular flow in normal and hypertensive persons, in Duke Hospital, Durham, N. C.; Lutfu L. Uzman, Istanbul, Turkey, isolation and characterization of brain proteins and their role in health, disease and senescence, at McLean Hospital, Waverley, Mass.; John M. Weller, Hines, Ill., ionic patterns of the intracellular fluids nad their influence on enzymatic reactions, at Harvard Medical School, Boston.

National Research Council Grants in Endocrinology.—The Committee on Research in Endocrinology, National Research Council, announces that requests for grants-in-aid during the fiscal year July 1, 1948 to June 30, 1949 will be received until Feb. 29, 1948. Application blanks may be obtained by addressing the Secretary, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. In addition to a statement of the problem and research program, the committee desires information regarding the proposed method of attack, the institutional support of the investigation and the uses to be made of the sum requested. No part of any grant may be used by the recipient for administrative expenses. The committee makes grants in aid of research in the general field of experimental and clinical endocrinology. However, applications for support of research in the problems of sex in the narrower sense cannot be given favorable consideration, and investigators who seek support in this field should direct their proposals to the Committee for Research in Problems of Sex, National Research Council.

Annual Meeting of Orthopaedic Surgeons.—The American Academy of Orthopaedic Surgeons will hold its fifteenth annual meeting January 24-29 at the Palmer House, Chicago, under the presidency of Dr. Rexford L. Diveley, Kansas City, Mo. Among others, four distinguished foreign guests will speak: Dr. H. Osmond-Clarke, London, England, "Fractures of the Carpal Scaphoid"; Dr. Sten Friberg, Stockholm, Sweden, "The Problem of the Lumbar Intervertebral Disk—Some Pathologic and Clinical Aspects"; Professor Jacques Leveuf, Paris, France, "Treatment of the 'True' Congenital Luxation of the Hip. Results of the 'Open Reduction'," and Dr. Robert M D'Aubigne, Paris, "Surgical Treatment of Nonunion of Long Bones." Numerous members of the academy and their guests will present thirty papers. On the Tuesday morning program is a symposium on Orthopedic Rehabilitation. A series of thirty-five instructional courses will be given beginning Sunday at 2 p.m. Seminars and cadaver demonstrations in anatomy have been added this year. The Audiovisual Program opens at 2 p.m. Saturday. There will also be scientific and technical exhibits. The annual dinner and dance will be Wednesday evening at 7:30.

FOREIGN

Postgraduate Summer School.—A Postgraduate Summer School will be held at the Medical School of the University of Birmingham, Birmingham, England, from July 10 to August 7, presenting courses on the physiology of sex hormones, fat absorption in experimental animals and man, and lipoprotein association in biologic systems. The school is intended for graduates who have done advanced work in the appropriate fields of science and medicine; it is open to men and women. The fee is £44 for board, residence and tuition. Applications from American students should be sent to the Director, Institute of International Education, 2 West 45th Street, New York 19, by March 15, 1948. The envelope should be marked "Birmingham University Medical Summer School."

Traveling Fellows from India.—Dr. Natesaier Purshottan, a pediatrician, and his wife Tara Deodhar Purshotten, a biochemist, of India are traveling throughout the United States on six months' fellowships from the United Nations, to observe particularly our methods of organizing public nutrition programs. Dr. Purshottan's ambition is to organize school lunchrooms based on American models throughout India, as only two cities in his country have school lunch programs at present. The new Indian government has established a Ministry of Health, and one of its first objectives will be better health for children, most of whom now are undernourished. The Purshottans recently visited the U. S. Public Health Service headquarters in Washington, D. C., where they were particularly interested in the nutrition surveys which that agency is conducting in communities in four areas of the United States and which are designed for the dual purpose of collecting data on the prevalence of deficiency disease and demonstrating methods for using the recent developments in the science of nutrition to prevent illness.

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Marriages

HENRY CARL MESSERSCHMIDT JR., Richmond, Va., to Miss Betty Rowland Fidler of Burlington, N. C., Nov. 15, 1947.

JAMES WARREN WIDEMAN JR., Manning, S. C., to Miss Lillian Heyward Evans of Raleigh, N. C., Oct. 25, 1947.

JOHN J. HANLON JR., Harrisburg, Pa., to Miss Doris Marie Patrick of New Cumberland, Nov. 8, 1947.

FREDERIC PRATT HERTER, Boston, to Miss Harriet Ames Conel of Newton, Mass., Nov. 22, 1947.

JOSEPH L. STECHER, Baltimore, to Miss Hazel Heinmiller of Orlando, Fla., Oct. 18, 1947.

MILTON HAMLIN BLAND to Miss Joyce Elaine Gagner, both of Norfolk, Va., Oct. 25, 1947.

CHESTER CASSEL, Miami, Fla., to Miss Carol Isaacson of New York, Dec. 19, 1947.

EMANUEL CHUSID to Miss Alta Butkus, both of Chicago, Dec. 13, 1947.

Deaths

Frederic Ewald Sondern ✠ New York; born in Stuttgart, Germany, March 30, 1867; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; an Affiliate Fellow of the American Medical Association, serving as a member of the House of Delegates from 1916 to 1921 and from 1932 to 1942; past president and formerly treasurer of the Medical Society of the State of New York; past president of the Medical Society of the County of New York; emeritus professor of clinical pathology and past president at the New York Post-Graduate Medical School and Hospital, Columbia University; served on the staffs of the Roosevelt, Bellevue and New York Lying-In hospitals; died in the New York Post-Graduate Medical School and Hospital Oct. 10, 1947, aged 80.

Christopher Adam Henry Arnecke ✠ Arneckeville, Texas; University of the South Medical Department, Sewanee, Tenn., 1895; died Sept. 2, 1947, aged 87, of coronary occlusion.

Theodorus Bailey, New York; Columbia University College of Physicians and Surgeons, New York, 1899; at one time instructor at the New York Polyclinic; served on the staff of Manhattan State Hospital; died in Dania, Fla., Sept. 25, 1947, aged 72, of coronary occlusion.

William Augustus Ball ✠ Wanette, Okla.; Chattanooga (Tenn.) Medical College, 1897; died recently, aged 74, of hypertension.

Daniel Bradley Brinsmade ✠ Major, U. S. Army, retired, Belmont, Mass.; Columbia University College of Physicians and Surgeons, New York, 1900; entered the medical corps of the U. S. Army in 1920; retired Nov. 30, 1933 for disability in line of duty; served in France during World War I; at one time surgeon in charge of the Watertown (Mass.) Arsenal; died Sept. 25, 1947, aged 73, of cerebral hemorrhage.

William Henry Burgess ✠ Orlando, Fla.; Louisville (Ky.) Medical College, 1907; at one time practiced in Williamson, W. Va.; member of the West Virginia State Medical Association; died Oct. 7, 1947, aged 80, of heart disease.

William James Burgess, Verona, N. J.; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1901; affiliated with the Essex Mountain Sanatorium; died in St. Francis Hospital, Burlington, Iowa, Oct. 1, 1947, aged 69, of carcinoma of the bladder.

Charles Elbert Byler, Lepanto, Ark.; University of Tennessee College of Medicine, Memphis, 1914; died Sept. 23, 1947, aged 60, of coronary occlusion.

Edgar M. Carman, Vashti, Texas (licensed in Texas under the Act of 1907); member of the American Medical Association; died in Gladstone, N. Mex., recently, aged 75, of angina pectoris.

Albert C. Chenoweth, Huntington, Ind.; Hahnemann Medical College and Hospital, Chicago, 1908; died Oct. 6, 1947, aged 70, of cerebral hemorrhage.

Alvin Harvey Chilson, Plymouth, Iowa; State University of Iowa College of Medicine, Iowa City, 1913; member of the American Medical Association; died in Cherokee recently, aged 62, of chronic myocarditis.

Clifton Mather Cooley ✠ New Britain, Conn.; Yale University School of Medicine, New Haven, 1908; vice chairman of the appeal board and a member of the draft board during World War I; served as medical examiner for the city of New Britain; affiliated with New Britain General Hospital, where he died Sept. 5, 1947, aged 66.

Okey Warren Coplin, Elizabeth, W. Va. (licensed in West Virginia in 1902); served as county health officer and county sheriff; died in St. Joseph's Hospital at Parkersburg, Oct. 6, 1947, aged 71, of cerebral hemorrhage.

James H. Edgar, Richland, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1900; died recently, aged 73, of chronic myocarditis.

Gayfree Ellison, Pawhuska, Okla.; born in Norman, Okla., June 25, 1916; University of Oklahoma School of Medicine, Oklahoma City, 1940; member of the American Medical Association; interned at Baltimore City Hospital; served two years in Europe, Africa and the Middle East during World War II; awarded the Bronze Star Medal, five battle stars and the American Defense Medal; formerly on the staff of the State Hospital in Clinton; was found dead Sept. 18, 1947, aged 31.

Robert Conway Finlay, Glen Allan, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1909; member of the American Medical Association; served on staff of King's Daughters' Hospital, Greenville; died Oct. 16, 1947, aged 63, of diabetes mellitus and obliterative endarteritis.

Minnetta C. Flinn-Jordan ✠ Wabash, Ind.; University of Michigan Homeopathic Medical School, Ann Arbor, 1905; died Sept. 25, 1947, aged 78.

Ashby Floyd, Phenix City, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1892; served on the school board, as city commissioner and as mayor; city recorder; died Oct. 3, 1947, aged 81.

Robert David Furlong, University City, Mo.; St. Louis University School of Medicine, 1933; served with the U. S. Public Health Service Reserve of the Coast Guard during World War II; affiliated with St. Mary's Hospital, Josephine Heitkamp Memorial Hospital, Jewish Hospital and the Missouri Baptist Hospital; died Oct. 24, 1947, aged 36, of coronary occlusion.

Paul Middleton Gamble, Albert Lea, Minn.; University of Minnesota Medical School, Minneapolis, 1924; member of the American Medical Association; died Sept. 14, 1947, aged 49, of carcinoma of the right lung.

William Ginsberg ✠ St. Paul; University of Minnesota Medical School, Minneapolis, 1915; served overseas during World War I; major, medical reserve corps, not on active duty; on the staffs of St. Luke's, St. Joseph's and Miller hospitals; died Sept. 21, 1947, aged 57, of acute coronary occlusion and hypertension.

Hyman Maurice Glasston ✠ Linden, N. J.; University of Vermont College of Medicine, Burlington, 1924; served during World War I; formerly physician for the board of health, board of education and fire department; for many years a trustee of the public library; served on the staffs of the Elizabeth General and St. Elizabeth's hospitals in Elizabeth, N. J.; died in New York Oct. 19, 1947, aged 47, of coronary disease.

Margaret Ann Gould ✠ Pittsburgh; Trinity Medical College, Toronto, Canada, 1898; an Affiliate Fellow of the American Medical Association; died Oct. 30, 1947, aged 77.

Irving Greenberg ✠ South Fallsburg, N. Y.; University and Bellevue Hospital Medical College, New York, 1917; died Oct. 13, 1947, aged 54, of cerebral hemorrhage and arteriosclerosis.

Thomas S. Grissom, Mount Pleasant, Texas; Memphis (Tenn.) Hospital Medical College, 1900; president of the Titus County Medical Society; died Sept. 27, 1947, aged 75, of congestive heart disease.

Frederick Grunwald, Louisville, Ky.; Kentucky School of Medicine, Louisville, 1898; member of the American Medical Association; served overseas during World War I; major, medical reserve corps, U. S. Army, not on active duty; for many years on the staff of the SS. Mary and Elizabeth Hospital, where he died Sept. 25, 1947, aged 73.

Robert Lee Hagaman, Raymond, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1891; affiliated with the Baptist Hospital, Jackson, where he died Oct. 15, 1947, aged 81, of myocardial failure.

Allen Richmond Howard ✠ Major, U. S. Army, retired, North Attleboro, Mass.; Cooper Medical College, San Francisco, 1911; Army Medical School, 1917; entered the medical corps as a first lieutenant in 1917; served during World War I; retired July 31, 1929 after twelve years' service; served on the staffs of the Washingtonian Hospital in Boston and the Sturdy Memorial Hospital in Attleboro; died June 4, 1947, aged 60, of coronary occlusion.

Winfred Lewis Howe, Everett, Mass.; Tufts College Medical School, Boston, 1900; member of the American Medical Association; chairman of the school committee and board of health; affiliated with the Massachusetts Memorial Hospital, Boston; died recently, aged 72, of arteriosclerotic heart disease.

Theodore Johnston ✠ Chicago; Bennett Medical College, Chicago, 1905; formerly professor of anatomy at his alma mater; for many years physician for the Atchison, Topeka and Santa Fe Hospital Association; died in Evangelical Hospital, Oct. 12, 1947, aged 73, of chronic myocarditis and arteriosclerosis.

Wayne Theodore Killian ✠ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1906; professor emeritus of anesthesia at his alma mater; member of the American Society of Anesthetists; past president of the Medical Club of Philadelphia; for many years on the staff of Hahnemann Hospital, where he died Oct. 11, 1947, aged 68, of myocardial infection.

George Franklin Lamb ✠ Grand Rapids, Mich.; University of Toronto Faculty of Medicine, Toronto, Canada, 1903; served during World War I; on the staffs of Blodgett and St. Mary's hospitals; died Oct. 6, 1947, aged 74, of carcinoma of the colon.

George Rufus Leonard, Chicago; Indiana University School of Medicine, Indianapolis, 1908; on the staff of Ravenswood Hospital; died Oct. 30, 1947, aged 70, of heart disease.

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George B. Lowrie, Detroit; Detroit College of Medicine, 1900; member of the American Medical Association; for many years on the staff of the Harper Hospital; chief surgeon for the Michigan Central Railroad; served on the faculty of his alma mater; died Sept. 21, 1947, aged 73.

Orban Gayle McConnell ✠ San Jose, Calif.; Washington University School of Medicine, St. Louis, 1924; served as a first lieutenant in the U. S. Army during World War I; medical examiner and inspector of selective service during World War II; on the staff of the O'Connor Sanitarium; died Sept. 21, 1947, aged 57, of injuries received in an automobile accident.

Edmund Johnson McNeil, Cambridge, Mass.; Tufts College Medical School, Boston, 1903; died recently, aged 75, of arteriosclerosis.

Robert Jack Mitchell ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1901; died in St. Luke's Hospital Sept. 15, 1947, aged 69.

Harold Alphonsus Murphy ✠ Boston; Tufts College Medical School, Boston, 1915; died Sept. 23, 1947, aged 56, of carcinoma of the stomach.

Carlton Maurice Neiberg, Pittsburgh; University of Illinois College of Medicine, Chicago, 1925; specialist certified by the American Board of Orthopedic Surgery; member of the American Medical Association and American Academy of Orthopedic Surgeons; on the staffs of Columbia, Children's and Pittsburgh hospitals, died Sept. 25, 1947, aged 47.

Philip Lawrence Patrick ✠ Marceline, Mo.; Washington University School of Medicine, St. Louis, 1902; past president of the Linn County Medical Society; served during World War I; died Sept. 19, 1946, aged 71, of cerebral hemorrhage.

James V. Prewitt, West Point, Ky.; St. Louis College of Physicians and Surgeons, 1889; died Oct. 9, 1947, aged 84, of chronic myocarditis.

John Marvin Proctor ✠ Hot Springs National Park, Ark.; University of Tennessee Medical Department, Nashville, 1906; served as a member of the state board of health; councilor of the Seventh District of the Arkansas Medical Society; died recently, aged 69, of abdominal hemorrhage.

Charles Armand Rabethge, Randolph, Mass.; College of Physicians and Surgeons, Boston, 1891; Jefferson Medical College of Philadelphia, 1894; University of Michigan Homeopathic Medical School, Ann Arbor, 1898; died Sept. 17, 1947, aged 85.

John Dexter Rice, West Boylston, Mass.; Tufts College Medical School, Boston, 1940; interned at the Worcester City Hospital in Worcester, Mass., and served a residency at the Massachusetts Eye and Ear Infirmary in Boston; diplomate of the National Board of Medical Examiners; killed Oct. 4, 1947, aged 32, in an automobile accident near Bowling Green, Ohio.

Mary Ann Nutting-Sanborn, Meredith, N. H.; College of Physicians and Surgeons, Boston, 1890; died Sept. 6, 1947, aged 85.

John Wilson Sayer, Watertown, N. Y.; Syracuse University College of Medicine, 1935; member of the American Medical Association; interned at St. Vincent's Hospital in Staten Island and served a residency at the Flower and Fifth Avenue Hospitals in New York; on duty in the European theater of operations during World War II; found dead Sept. 25, 1947, aged 37.

Keith Sears, Trumansburg, N. Y.; Cornell University Medical College, New York, 1903; died Sept. 10, 1947, aged 70.

James M. Seliskar, Cleveland; Western Reserve University Medical Department, Cleveland, 1905; affiliated with Charity Hospital; died Sept. 23, 1947, aged 67, of arteriosclerosis.

Foster Clarke Shaffer ✠ Douglas, Wyo.; Jefferson Medical College of Philadelphia, 1925; served as a member of the board of examiners; for eight years member of the city council; for many years a member of the school board and a health officer; died recently, aged 46, of heart disease.

Herbert D. Sterrett, Hutchinson, Kan.; Ensworth Medical College, St. Joseph, Mo., 1899; University of Kansas School of Medicine, Kansas City, Kan., 1906; died recently, aged 70, of leukemia.

August Strauch, Chicago; Medizinische Fakultät der Universität Wien, Austria, 1898; formerly on the faculty of Rush Medical College; served on the staff of Cook County Hospital; died Oct. 13, 1947, aged 74.

James Porter Strickler ✠ Scottdale, Pa.; Jefferson Medical College of Philadelphia, 1901; died recently, aged 69, of cerebral thrombosis.

Oscar F. Sugg, Corydon, Ky. (licensed in Tennessee in 1896); died Oct. 14, 1947, aged 88, of myocarditis.

Samuel Sullivan, Chicago; Dearborn Medical College, Chicago, 1907; served during World War I; died Oct. 8, 1947, aged 71.

Edward Eugene Terrell, Cranford, N. J.; University of Chicago School of Medicine, 1931; member of the American Medical Association; interned at the New Haven (Conn.) Hospital; formerly resident physician at the Rockefeller Institute for Medical Research in New York; served in the Southwest Pacific during World War II; for many years school physician; on the staff of the Muhlenberg Hospital in Plainfield, where he died Oct. 2, 1947, aged 44, of acute nephrosis and pneumonia.

U. G. Mitchell Walker, Flint, Texas (licensed in Texas under the Act of 1907); member of the American Medical Association; died in a hospital at Jacksonville recently, aged 77, of pulmonary edema.

Thomas John Walshe, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1897; member of the American Medical Association; served on the staffs of the Charity Hospital and the Southern Baptist Hospital, where he died recently, aged 71, of coronary thrombosis.

Joseph P. Wilson ✠ Scottsburg, Ind.; Kentucky University Medical Department, Louisville, 1905; secretary of the Scott County Medical Society; county physician; died Sept. 23, 1947, aged 82, of coronary thrombosis.

William Price Womack, Shelbyville, Tenn; University of Tennessee College of Medicine, Memphis, 1933; interned at Baptist Memorial Hospital in Memphis; died Sept. 15, 1947, aged 43, of hypertension with acute heart failure.

DIED WHILE IN MILITARY SERVICE

Lavin Milford Andersen, Manistee, Mich.; University of Michigan Medical School, Ann Arbor, 1924; served an internship and residency at the Long Island College Hospital in Brooklyn, where he served as assistant clinical professor of radiology; formerly on the staffs of the Brooklyn Eye and Ear, the Samaritan and the Midwood hospitals, all in Brooklyn; specialist certified by the American Board of Radiology; began active duty as a major in the medical corps, Army of the United States, in October 1942; stationed at Camp Myles Standish at Taunton, Mass., and at Camp Butner, N. C., where he died Sept. 9, 1945, aged 46, following a gallbladder operation.

Melvin Denver Deck, Provo, Utah; Washington University School of Medicine, St. Louis, 1943; interned at Minneapolis General Hospital in Minneapolis; began active duty as a first lieutenant in the medical corps, Army of the United States, on March 2, 1944; stationed at the Medical Department Replacement Pool, Stark General Hospital, Charleston, S. C., with temporary duty at the Medical Field Service School, Carlisle Barracks, Pa.; relieved from duty at Stark and assigned to duty with the 133d General Hospital, Camp Gordon, Ga., in May 1944; subsequently went overseas with that unit; promoted to captain; killed in the Pacific area off Leyte Sept. 6, 1945, aged 29, while a passenger on a C-47 (skytrain) transport plane.

Emanuel Dejnozka Jr., Rock City Falls, N. Y.; born in New York, July 26, 1916; Albany Medical College, 1942; diplomate of the National Board of Medical Examiners; interned at Misericordia Hospital in New York; appointed first lieutenant in the medical department, Army of the United States, June 4, 1942 and began active duty July 3, 1943; assigned to Station Hospital and the 3706th Army Air Forces Base Unit at Sheppard Field, Texas; promoted to captain; on July 9, 1945 arrived in the European theater of operations, where he was assigned to headquarters, 9th Air Disarmament Group, 53d Air Disarmament Squadron and 1515th Quartermaster Battalion; died Dec. 4, 1945, aged 29, of injuries received when the ambulance in which he was riding near Walsdorf, Germany, skidded and went over an embankment.

Homer LaFayette Hobbs, Greensboro, N. C.; Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., 1944; interned at the Paterson (N. J.) General Hospital; entered the medical corps of the Army of the United States as a first lieutenant on July 6, 1945; killed in an automobile accident in Harrisburg, Pa., April 16, 1946, aged 27.

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Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 30, 1947.

The British Medical Association and the National Health Service

In a letter to the *Daily Telegraph* Sir Ernest Graham-Little, dermatologist and member of Parliament, who is the great protagonist of a state medical service, has summed up the present position. He first points out the reluctant consent of the Minister of Health, Mr. Bevan, to consult with the members of the medical profession on the scheme. As he sees it, the medical profession, under the leadership of the British Medical Association, demands a radical amendment of the National Health Service Act as a preliminary to accepting service under the act. It is therefore important to consider the strength and influence of the British Medical Association. Four years ago its membership was about 40,000; today it is 56,000. Some 70,000 practitioners are on the medical register, but only about 50,000 are in practice. It is clear that the present membership includes practically all those who are in active practice, a record of special significance, as membership is voluntary.

The promised medical service will call for medical staffing twice or thrice as large as the existing number of active practitioners. It takes six years to train a general practitioner and from ten to twelve years to train a specialist. Thus the law cannot be properly enforced for two or three decades, if at all. Meanwhile, the existing health services, admitted to be among the best in the world, will be completely disrupted. Therefore it is not surprising that Mr. Bevan should be reluctant to disclose the actual available resources with which he proposes to launch the act within the next eight months. The National Health Service is now law, and the government proposes to put it into operation soon, but negotiations between the British Medical Association and the government are still proceeding. These have not been disclosed, though concern regarding them has been expressed. The medical profession has been assured that its representatives are making a firm stand on the demand that the act should be amended according to its wishes. The increased membership of the British Medical Association, due to apprehensions aroused in the profession by attempts to socialize the practice of medicine, has strengthened its position in its struggle with the government. Its claim to represent practically the whole active membership of the profession cannot now be gainsaid.

Research on Cancer

At the annual meeting of the British Empire Cancer Campaign the Duke of Gloucester stated that $540,000, a record sum, had been collected in the past financial year. If additional funds were available progress could be greatly speeded up; more of the best brains in the Empire could be attracted to cancer research, and the equipment of research centers could be much improved—all of which would go far toward hastening the conquest of cancer, which is now the chief killing disease. The number of deaths due to cancer of the lung have increased sixteen and one-half times in men and eight times in women since 1921, although the incidence of cancer of the larynx has not increased in either sex in the last fifteen years. Some authorities consider that the apparent increase in cancer of the lung is due wholly to improved methods of diagnosis, while others emphasize the high proportion of error which allows over 40 per cent of cases to escape diagnosis even under the best conditions of hospital practice. The examination of sixty-five occupations has disclosed none which account for any large fraction of the increase of deaths attributed to cancer of the lung.

The Journal of Clinical Pathology

The British Medical Association announces the publication of a new periodical, the *Journal of Clinical Pathology*. It will consist of original articles, reviews, technical methods and abstracts which will be useful to practicing clinical pathologists, whose chief concern is to elucidate disease in man. The editor is Dr. A. Gordon Signy, who has been appointed by the Association of Clinical Pathologists. The journal will be published quarterly, and the subscription is $6 per annum.

The Virus Question

Lord Horder said that a special committee has been set up to develop research into the whole position of virus in relation to cancer, and a grant of $100,000 has been set aside for the purpose. The view that cancer lay outside the scope of chemotherapy was probably premature. Recent work has been quite hopeful, and the campaign appointed another special committee to organize research in this field. In the field of physics atomic energy has brought new tools of use in research and treatment.

ITALY

(From Our Regular Correspondent)

Nov. 15, 1947.

Effect of Ascorbic Acid on Intradermal Tuberculin Reaction

At a meeting of the Ferrara section of the Italian Society of Experimental Biology, Dr. C. Mattei, of the Institute of Medical Pathology of the University of Ferrara, reported on the changes in the intradermal tuberculin reaction in persons to whom ascorbic acid had been administered. His research was aimed to demonstrate one aspect of the immunizing action of ascorbic acid. The method employed was to produce on one forearm an intradermal reaction with Koch's old tuberculin before treatment with ascorbic acid and to produce an analogous elevated patch on the other forearm with distilled water. At intervals of fifteen minutes, twelve hours and twenty-four hours, the outline of the zone was examined through a small sheet of cellophane; an elevated red spot was clearly visible. The area involved was measured. The number indicating in millimeters the extent of the elevated patch has been defined as the "tuberculin value." Then the organism was loaded with ascorbic acid by intravenous administration, until a state of saturation was reached, as determined by the amount of ascorbic acid excreted daily in the urine, using dichlorophenolindophenol.

Treatment was given to 21 patients divided in three groups: patients with hepatic disorders, patients with tuberculosis and patients with various disorders. All the patients had suffered with malaria. Results were as follows: in the group with hepatic disorders the medium tuberculin value was increased from 61 before the administration of ascorbic acid to 140 after its administration (140 per cent). In the group with tuberculosis the increase was from 61 to 84 (38 per cent), and in the group with various disorders from 99 to 163 (65 per cent). In only 5 of the 21 patients who were treated was a reduction of the tuberculin values observed with medium variations of less than 35 per cent.

The results of Mattei's research thus demonstrated that in the majority of cases the saturation of the organism with ascorbic acid determined an increase in the intensity of the intradermal reaction after the injection of tuberculin.

Sulfonamide Compounds and Penicillin

At a meeting of the Roman Medicosurgical Association in Ravenna, Dr. L. Fontana presented the results obtained by him with sulfonamide compounds and penicillin when administered by the intrapleural and the intra-articular route. The speaker reported highly satisfactory results in many cases, even of the multilocular type, of empyema by means of intrapleural injec-

tions of sulfonamide compounds (sulfapyridine and sulfathiazole) after previous removal of a certain amount of pus. He reported instances of definite and fairly rapid recovery. After penicillin came on the market, Dr. Fontana adopted the intrapleural injection in doses of 50,000 to 100,000 units combined in general with the administration of sulfonamide compounds, and he has obtained highly satisfactory results. For pulmonary abscess and gangrene the speaker considered penicillin by the endobronchial route and by means of bronchoscopy the method of choice, particularly in the many cases which are inaccessible by the transthoracic route, but he did not have direct experience. Excellent results were obtained also in cases of suppurative arthritis with intra-articular injections of sulfonamide compounds or penicillin after previous removal of pus. Rapid and definite improvement occurred with few and temporary functional residues.

Dr. Galassi reported the results obtained with transthoracic intrafocal injections of penicillin in the treatment of pulmonary abscess. The technic was in principle the same as that used by other authors, i. e., entering the lung under roentgenologic control and from there the cavity of the abscess. Among the inconveniences manifested during such trials, the most important was the production of a pneumothorax in 1 instance, which, however, subsided spontaneously within a short time. From the small number of cases so far observed, Dr. Galassi has not been able to draw definite conclusions, but he considers the intrafocal treatment of pulmonary abscess with penicillin as promising.

SPAIN

(From Our Regular Correspondent)

MADRID, Nov. 18, 1947.

History of Anatomy

At the Madrid Medical Association, an interesting course of lectures has been given by Dr. P. Lain Entralgo, who has brilliantly succeeded in the Chair of History of Medicine of the Madrid Faculty the now retired Dr. E. Garcia del Real. The object was to present Dr. Lain's concept of the historical evolution of anatomy, whose basic stages are represented, according to him, by Galenus, Vesalius, Bichat, Virchow and Gegenbaur, passing through the interlude of Testut, to end in Braus's "Anatomie des Menschen."

In his survey Lain passed successively through the following considerations: if the anatomist proposes to describe the external appearance and the internal structure of man, it is evident that man presents two fundamental constituent signs: the external and internal form of the body and the movement of that body which displays his living activity, which signs had perforce to mark rules, norms of thought, for the first Greek anatomists. Hence the first anatomic vision, faithful to the cultural lines of Greece, was that of Galenus, who described the body as a living anatomy.

The following stage is represented by Vesalius, who, during the Italian Renaissance and himself a perfect dissector of (motionless) corpses, describes these as though they were immobile statues with only potential movement. Therefore his anatomic concept is architectural and static. For this reason, he—an innovator in anatomy but a traditionalist in physiology—describes, in his "De Fabrica Humani Corporis," the human statue as potentially—only potentially—animated by the three old Dynameis of classical physiology.

That static anatomic body of Vesalius' is first put into movement by the physiologists, who appear in the course of time: Fabricius ab Aquapendente, Sanctorius, Harvey and Borelli. The forces and laws which will put it into operation will no longer be Galenus's old Dynameis but those indicated by the new physiologic knowledge.

In the eighteenth century Bichat begins to see the body no longer as a static unit ready to move but as a whole composed of parts, which are the tissues, harmoniously related in the vital conjunction. What in Vesalius was an architectural element is replaced in Bichat by the tissues of every element, in which reside the specific forces of the vital activity.

Fifty years later Virchow, with the microscope already available and two contributions brought by time: the genetic idea and individualism—which will act and influence him as the atmosphere of the time—will see a cell where Bichat saw a tissue. Cellular pathology, which Virchow explains, is, Lain said: "a federal republic of vital units: the cells grouped into tissues, organs and systems." Bichat and, above all, Virchow then attempt to give an analytic explanation in exclusively anatomic descriptions, forgetting the real form of the body as the human eye sees it.

In this situation Gegenbaur appeared, "the anatomist who most genuinely projected on anatomic description the idea of the evolution of living beings," "making anatomy scientific by means of genetic explanation" without giving up the cellular theory. Gegenbaur focused anatomic study, investigating the steps made by the body previously, and came to conceive the human body —its form—as "the occasional and transitory state of an evolution, of a progressive process toward more complex and perfect biologic states." But Gegenbaur proceeded in the Vesalian manner: he studied the parts of the body, the organs and the tissues, separately in the first chapters of his work.

From this panoramic view of Lain's we infer that Galenus, Vesalius, Bichat, Virchow and Gegenbaur are the representatives of the various ways of looking at the human body throughout history and that their names may be used to designate the respective interpretations: each of them represents in anatomy the cultural panorama of the respective historical situation, not only because the means of observation were different at every moment in history but because the descriptive mentality of each period differed.

The anatomic vision of today is not, according to Lain, that of Testut, which looks like a game, but that represented by Braus. Braus's "Anatomy" is, in a certain way, a "return to Galenus"—his descriptive point of view is functional or physiologic—although, naturally, without giving up the ulterior tectologic and evaluative points of view. Braus attempts, not always successfully, to reduce to systematic unity the functional, tectologic and genetic consideration of human anatomy.

This course was attended by large audiences who listened to Professor Lain Entralgo with evident admiration. In the Spanish medical culture of the present, Lain Entralgo represents the intellectual sign of the times, giving to the history of medicine intellectual and philosophic contents which, at his age, can only be found in one as well endowed personally as he is.

These data are advanced to readers of THE JOURNAL because of the great interest awakened by their exposition in the Spanish public, always avid for weighty concepts, and because of the impetus now being given to historical studies by this master who is little known abroad.

Of his lectures, he has so far published monographically only the one on Bichat.

Congress of Digestive Pathology and Nutrition

The fifth Spanish Congress of Digestive Pathology and Nutrition was held in Saragossa October 26-30. The first report was read by Dr. C. Jimenez Diaz, professor in the Madrid Faculty of Medicine, and his collaborator Dr. Marina Fiol on "Chronic Enteropathy of the Liver." More about this paper will appear in another letter, because it was of great interest.

The second report, by Professor J. Andreu Urra, of Seville University, dealt with "The Influence of the Midbrain and the Pituitary Body on Glucide Metabolism." Dr. Andreu summed up his experimental work of a number of years, coming to highly interesting conclusions.

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The subject "Problems of Chronic Appendicitis" was expounded by Drs. Pinos and Pi-Figueras, and the fourth report, by Professor G. Maranon, on "Thinness, Its Pathogenesis and Treatment" was read in summarized form by Dr. Gutterrez Arrese in the author's absence.

During the congress, meetings were held by the sections of digestive pathology, nutrition, surgery and therapeutics and diagnosis, in the course of which some two hundred communications were heard.

Professor Bonorino Udaondo, of the Buenos Aires (Argentina) Faculty of Medicine, lectured on "Intestinal Polyposis"; Professor Teofilo Hernando on "Intestinal Tuberculosis," and Dr. Callar Mones, of Barcelona, on "Medical and Surgical Treatment of Gastroduodenal Ulcer." The Congress had an extraordinarily large attendance of specialists. The next congress will be in Santander in 1950.

Improvements at Seville

The Seville Faculty of Medicine has been greatly improved. About a year ago an Institute of Anatomy was opened, and now another building is being erected to house the Departments of Physiology, Biochemistry, Pharmacology and Microbiology. Another building is under construction for a new Polyclinic Institute. Although the Old Central Hospital annexed to the Faculty of Medicine is out of date, it is being gradually renewed. Nevertheless, the city still lacks a modern hospital such as a university city of its rank should have.

The most significant work done in the Medical Schools of Seville University in recent years is that of Professor J. Andreu Urra's School, on clinical and experimental lines, on the influence of the midbrain and the pituitary body in carbohydrate metabolism. Dr. Andreu directs an excellent school in which studies are conducted notwithstanding the difficulties arising from a shortage of materials. In his school papers have also been published on the origin of the proteins of the plasma (Dr. Villar and collaborators) and on intestinal absorption (Dr. Leon Castro); another is now being prepared by the latter author on immunity.

The Seville Royal Academy of Medicine, whose president is Dr. Dominguez Rodino, maintains a permanent state of activity, being a center for meetings and lectures, and so does the Seville Royal Medical Society of Hospitals, which was directed by Professor P. Rodrigo Sabalette up to the time of his death.

To sum up, the medical scientific activity of Seville is on the increase and carries on at a promising pace. It is expected that when material contributions and working conditions improve the Seville Schools will attain to the greatest fame in Spain.

Professor P. Rodrigo Sabalette

In the terrible explosion in the torpedo dump at the Cadiz naval yards, Professor P. Rodrigo Sabalette died in the prime of life with two of his sons. Professor Rodrigo Sabalette was one of the most distinguished figures in Spanish medicine. A son of Professor L. Rodrigo Lavin (a great Spanish physiologist who, at 80 years of age, is thus bereft) he studied in England and Germany mostly on problems of neurologic physiology. In recent years he wrote the chapters on Diseases of the Nervous System in the "Treatise of Medical Pathology" published under the editorship of Professor M. Banuelos, in which he displayed a deep didactic sense and magnificent clinical and therapeutic training and knowledge. He was the author of a monograph on "Cancer of the Lung" and of an excellent paper on "Slow Endocarditis and Sepsis," and his last papers, on brain tumors, still unpublished, represent a notable advance in this field. He was an exemplary member of Spanish university life, and his fine character enabled him to overcome great difficulties in his profession. His fellow workers and pupils, who owed so much to the chivalrous conduct and teaching of this great master, will not easily find another to replace him.

COPENHAGEN

(From Our Regular Correspondent)

Dec. 9, 1947.

BCG Vaccination in European Countries by the Danish Red Cross

Since BCG vaccination was first adopted in Denmark in 1927, this measure has proved so effective that the vaccine has lately become an article for export, witness the work of Danish BCG teams in Poland, Jugoslavia, Hungary, Austria and the American and British zones in Germany. Each of these Red Cross teams consists of one physician and two nurses, and it is hoped that the present number of fifteen teams will ultimately be quadrupled. But as Denmark alone cannot provide as many as sixty doctors trained in BCG vaccination, some of the newer teams must be staffed by members who have come from the aforementioned countries to study the highly specialized anti-tuberculosis work in Denmark. It is hoped that Norway also will supply a certain number of BCG specialists. In the past half year about half a million persons have already been vaccinated, and in Jugoslavia, where the Danes have worked for nine months, the government has now taken over this work. In Poland, the first country visited by the Danish teams, practically every one over the age of 25 was found to be tuberculin positive and was therefore not eligible for BCG vaccination. Accordingly, attention is being concentrated on persons under this age. The Danish Red Cross enjoys the active support of the Danish Public Health Service and of the State Serum Institute in Copenhagen. The sum of 3,500,000 kroner has been earmarked by the Danish Red Cross for BCG vaccination abroad, and three aeroplanes have been purchased for the supply of fresh vaccine at short intervals to the various centers in which the teams happen to be working. It is calculated that the cost per head of this measure is only ½ krone (50 öre) and that each team can deal with 1,500 to 2,000 persons every day. The goal which has been set by the Danish Red Cross is a total of 1,000,000 vaccinations per month.

The Wartime Rise in the Danish Birth Rate

Why did the Danish birth rate rocket up during the war in spite of shortages of food, fuel, houses, domestic servants and much else supposed to influence fertility? In an attempt to answer this question, Carry Hedemann quotes the following figures: In 1939 there were 67,900 births and in 1940 there were 70,100. By 1946 this figure had jumped to 96,000. At this rate there would have been some 100,000 live births annually in a short time, but from August 1946 onward there was a decline instead of a further rise. Was the wartime rise due to the blackout and other restrictions which made married couples more homebound than in peacetime? But in Sweden, where the birth rate also rose definitely during the war, there was no blackout or "house arrest" forcing married couples to remain at home. Did the German troops contribute appreciably to the rise in the birth rate? To be sure, they sired some 4,000 to 5,000 children in Denmark, but these figures are but a small fraction of the total rise. Was it due to a passing vogue, the bearing of many children having become rather fashionable instead of a stupendous mistake and disgrace? What is plain is that the knowledge of contraceptives acquired by the public has not had such a devastating effect on the birth rate as their opponents would have us believe. High wages and a resulting sense of social security may well have played an important part, and with all these and many other factors possibly influencing the birth rate, we must deny ourselves the luxury of clearcut conclusions, contenting ourselves with the undeniable fact that the Danish birth rate went up during the war by leaps and bounds.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Boards in Specialties were published in THE JOURNAL, Jan. 3, page 58.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 22-24, 1948. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery 4.

ALASKA: * Juneau, March 2. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS: * *Examination.* Little Rock, June 3-4. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana.

CALIFORNIA: *Oral.* San Francisco, Jan. 17-18; Los Angeles, Feb. 28-29. *Written Examination.* Los Angeles, March 1-4. *Oral and Clinical Examination for Foreign Graduates.* Los Angeles, Feb. 29; San Francisco, June 6. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* March 9-10. Sec., Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic Examination.* Derby, March 9-10. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, Jan. 13-15. *Endorsement.* Dover, Jan. 20. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * *Reciprocity.* Washington, D. C., March 8. Sec., Commission on Licensure, Dr. G. C. Ruhland, 4130 E Municipal Bldg., Washington.

FLORIDA: * *Examination.* Jacksonville, June 29-30. *Reciprocity.* Jacksonville, June 28. Sec., Dr. Harold D. Van Schaick, 6675 Windsor Lane, La Gorce Island, Miami Beach 41.

HAWAII: *Examination.* Honolulu, Jan. 12-15, 1948. Sec., Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu, T. H.

IDAHO: Boise, Jan. 13-15. Sec., Miss Estella S. Mulliner, 355 State House, Boise.

INDIANA: *Examination.* Indianapolis, June 1948. Sec., Board of Medical Registration and Examination, Dr. Paul R. Tindall, K of P Bldg., Indianapolis.

IOWA: * *Examination.* Iowa City, March 15-17. Comm., Dr. Walter L. Bierring, Dept. of Health, Des Moines.

KANSAS: Kansas City, June 9-10. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: *Examination.* Louisville, June 16-18. Sec., Dr. P. E. Blackerby, 620 S. 3d St., Louisville.

MAINE: Portland, March 9-10. Sec., Board of Registration of Medicine, Dr. A. P. Leighton, 192 State St., Portland.

MARYLAND: *Medical Examination.* Baltimore, June 15-18. Sec.-Treas., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic Examination.* Baltimore, June 15-16. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: *Examination.* Boston, March 9-12. Sec., Board of Registration in Medicine, Dr. H. Q. Gallupe, 413 E State House, Boston.

MINNESOTA: * Minneapolis, Jan. 20-22. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: Jackson, June 1948. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: *Examination.* Kansas City, Jan. 19-21. Exec. Sec., Mr. John A. Hailey, P. O. Box 4, State Capitol Bldg., Jefferson City.

MONTANA: Helena, April 5-7. Sec., Dr. O. G. Klein, First Nat'l Bank Bldg., Helena.

NEVADA: Carson City, May 3. Sec., Dr. G. H. Ross, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: *Examination.* Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 15-17. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW YORK: *Examination.* Albany, Buffalo, New York, Syracuse, Feb 16-19. Sec., Dr. J. L. Lochner, Jr., Education Bldg., Albany

NORTH CAROLINA: *Endorsement.* Pinehurst, Jan. 12. Sec., Ivan Procter, 226 Hillsboro St., Raleigh.

OHIO: *Endorsement.* Columbus, April 6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

PENNSYLVANIA: *Examination.* Philadelphia, Jan. 13-16, 1948. Acting Sec., Board of Medical Education and Licensure. Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

SOUTH CAROLINA: *Written Examination,* Columbia, June 21-23. *Endorsement.* Feb. 2. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 20. Sec., State Board of Health, Dr. Gilbert Cottam, Capitol Bldg., Pierre.

TEXAS: Austin, Feb. 19-21. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

UTAH: *Examination.* Salt Lake City, June, 1948. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

VERMONT: *Examination.* Burlington, Feb. 5-6. Sec., Dr. F. J. Lawliss, Richford.

WASHINGTON: * *Examination.* Seattle, Jan. 19-21. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WEST VIRGINIA: Charleston, Jan. 12-14. Comm., Public Health Council, Dr. N. H. Dyer, State Capitol, Charleston 5.

WISCONSIN: * *Examination.* Madison, Jan. 13-15. *Reciprocity Oral.* Madison, Jan. 14. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: *Examination.* Cheyenne, Feb. 2. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: Juneau, Feb. 23-29. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 19-20. Sec., Dr. G. C. Ruhland, 4130 Municipal Bldg., Washington.

FLORIDA: *Examination.* June 5. Final date for filing application is May 23. Sec., Mr. M. W. Emmel, Univ. of Florida, Gainesville.

IOWA: Des Moines, Jan. 13, April 13, July 13, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

NEBRASKA: *Examination.* Omaha, Jan. 13-14. Dir., Dept. of Health, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: Spring 1948. Sec., Dr. Frank Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 6. Sec., Basic Science Examining Committee, Mr. C. D. Byrne, Univ. of Oregon, Eugene.

WASHINGTON: *Examination.* Seattle, Jan. 14-15. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Husband's Action for Loss of Services of Wife Caused by Malpractice.—The plaintiff filed suit for damages for loss of the services and companionship of his wife alleged to have been caused by the malpractice of the defendant physician. From an unfavorable ruling of the trial court, the defendant appealed to the Supreme Court of North Dakota.

In 1943 the defendant physician was engaged to take care of the plaintiff's wife during her pregnancy. Shortly before the time for delivery, which was to be by caesarean operation, the defendant advised the plaintiff's wife that she would not be able to have another baby except by caesarean operation and that a second or successive operation would be dangerous and detrimental to her health. Accordingly it was agreed that the defendant would perform a sterilization operation on the wife at the time of the delivery. This was done and the defendant was paid his fee therefor, the defendant representing that the operation had been successfully and properly performed. Subsequently the plaintiff and his wife, relying on the representation of the defendant and believing that he had properly performed such operation, engaged in normal sexual intercourse and in 1945 the wife again became pregnant. It was again necessary to make delivery by caesarean operation, and the wife suffered such loss of blood therefrom as to require blood transfusions and to gravely endanger her life. The second caesarean operation and the birth of the second child, in addition to the fear and shock suffered by the plaintiff's wife on discovering that the sterilization operation had been a failure, that she was pregnant and that she would again be compelled to have a caesarean operation, permanently impaired her health and rendered her highly nervous and mentally and physically unstable. As a result thereof the plaintiff was compelled to expend a considerable amount of money for medical and hospital care and nursing services for his wife and was and will be deprived of the services and companionship of his wife for a long time—all as a consequence, it is alleged, of the defendant's failure to perform the sterilization operation in a proper and skilful manner.

The defendant physician admitted that he was engaged to perform the medical and surgical services referred to but denied that they were performed negligently or carelessly. He further alleged that the statute of limitations provides, among other things, that actions for the recovery of damages resulting from malpractice must be commenced within two years after the cause of action has accrued, that this is an action for malpractice, that the cause of action accrued at the time the alleged

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negligent operation was performed on or about March 16, 1943 and that inasmuch as defendant's services as a physician and surgeon terminated prior to April 1, 1943 and this action was not brought until Nov. 10, 1945 it is barred by the statute.

The court discussed the distinction between an action for malpractice which accrues to the wife and an action for damages for loss of the wife's services because of such malpractice which accrues to the husband. Among other things, the court said that the gist of the husband's cause of action is the loss and expense sustained by him, and not the injuries sustained by her, even though her injuries were caused by the wrongful acts or negligence of another. Such loss and expense sustained by him are not merely items of damages but are essential to the cause of action itself. The two liabilities are distinct. Thus, the fact that the statute of limitations has run against the wife's cause of action will not necessarily prevent the husband from prosecuting his. A cause of action does not accrue, said the court, until the party owning it is entitled to begin and prosecute an action thereon; it accrues at the moment when he has a legal right to sue on it and no earlier. A husband has no right of action for the loss of services, society and companionship of his wife and incidental expense for her treatment and care until the loss of services, society and companionship actually occurs. The negligence of the defendant physician in the performance of the operation on the plaintiff's wife was an invasion of her rights, and any injury sustained by her as a result thereof constituted a tort on her but did not constitute a tort on the plaintiff. The actionable wrong against the plaintiff was the interference with his marital rights, depriving him of his wife's services, society and companionship and requiring expenditures by him for her medical treatment and care. These do not constitute mere items of damage in an action for negligence. They are essential to the cause of action itself, which cannot arise until such consequences have followed the injury.

According to the complaint the plaintiff's wife gave birth to a child on March 7, 1945. The loss of services, society and companionship and expenditures for medical treatment and care occurred after the plaintiff's wife became pregnant with the child so born on March 7, 1945. The present action was commenced Nov. 10, 1945, within two years after the plaintiff's cause of action accrued. The Supreme Court therefore held that the order of the trial court overruling the defendant's defense of the statute of limitations was proper.—*Milde v. Leigh, 28 N. W. (2d) 530 (N. D., 1947).*

Workmen's Compensation Acts: Employer's Liability for Physician's Malpractice.—The claimant was granted an award for compensation for an alleged industrial accident so the defendant industrial commission appealed to the Supreme Court of Colorado.

The claimant, a waitress handling food in a local restaurant, was directed by her employer to secure a health certificate and submitted herself to examination by a physician, who drew from her arm some blood for the purpose of making a blood test required by law. The lesion made by the physician became infected, and as a result of the disability thus created she was forced to leave her employment.

It is admitted that the claimant did sustain a physical injury and that it was the result of an accident. Whether or not this accident "arose out of and in the course of her employment," however, depends on the circumstances under which she submitted to the blood test.

The evidence showed that the claimant and other employees were ordered by their employer to have a blood test made. They were not directed to go to any particular physician but were advised that if they went to a certain doctor the charge for the tests would be $2 each. The claimant went to a physician of her own choosing for the test. The Colorado general assembly created the State Board of Health, which it empowered "To establish a uniform code of sanitary rules and regulations for the preparation, sale and serving of food." It also provided that the code of sanitary rules and regulations include medical examination of all restaurant employees handling food. Regulation 6 of the state board's laws, rules and regulations provides: "All persons engaged in the handling and preparation of food shall obtain a permit card from the State Board of Health. Application for a permit card shall be made on a form furnished by the board and shall include a report from a licensed physician stating that the applicant has been examined and found free of communicable disease. Examinations shall include a blood test and other laboratory reports as indicated."

It is apparent, said the court, that the employer was obligated by the state law to have the claimant obtain a health certificate. It was not his regulation or requirement, it was that of the state. The claimant was incapacitated by reason of her compliance therewith. Obviously, as the commission found, her accident did not arise out of and in the course of her employment. Continuing, the court said that it had found no cases involving the question here presented, but that cases where employees have been injured as a result of vaccination or inoculation present similar legal problems. What they hold is, that the right to compensation is determined by the construction placed on the phrase, "arising out of and in the course of employment," and its application to the facts in each particular case. Compensation was allowed in those cases in which the vaccination or inoculation was performed for the benefit of the employer and had been required by him. On the other hand, compensation was denied in those cases where it appeared that vaccination or inoculation was made necessary by reason of public requirement.

In the instant case the claimant was ordered by her employer to take the blood test but this he was legally obligated to do under the statute. The commission was right in finding that the claimant's accident did not arise out of and in the course of her employment. Accordingly the judgment in favor of the claimant was reversed.—*Industrial Commission v. Messinger, 181 P. (2d) 816 (Colo., 1947).*

Drunkenness: Admissibility in Evidence of Chemical Test Showing Amount of Alcohol in Blood.—The defendant was charged with a negligent homicide as a result of his operation of a motor vehicle. From a judgment of guilty and sentence thereon, the defendant appealed to the Municipal Court of Appeals for the District of Columbia.

While the defendant was at a hospital following the automobile accident, he was asked for a specimen of his urine, which could be tested to determine whether or not he was under the influence of alcohol at the time of the accident. One of the police officers warned him that the results of such a test could be used for or against him. The defendant then gave the specimen. At the trial the specimen was produced, properly identified, and the results of the test were admitted in evidence, over objection by the defendant. According to expert testimony the tests showed 0.22 per cent alcohol and established that the defendant was under the influence of alcohol at the time. The defendant did not contend that the specimen was not given voluntarily (there is absolutely no showing of duress, intimidation or entrapment) but that the giving of the specimen was the equivalent of a confession and was therefore protected by the privilege of the Fifth Amendment against self incrimination. In *Novak* v. *District of Columbia*, 49 A. (2d) 88, *J. A. M. A.* **134**:208 (May 10, 1947), which involved a rather analogous situation, the court did not decide whether the giving of the specimen for analysis was the same, from an evidentiary standpoint, as making a statement or confession. In the present case the Municipal Court of Appeals said that it must now decide the question on which it reserved decision in the Novak case. We hold, said the Court of Appeals, that in taking the specimen there was no violation of any rights guaranteed by the Constitution. The whole history of the privilege against self incrimination shows that it was designed to protect against testimonial compulsion. There was no such compulsion here. The evidence sought was whether the accused was under the influence of alcohol. He does not claim that the scientific test was inaccurate or that the results of the test were incorrectly interpreted. What is obtained from the accused by such action is not testimony about his body, said the court, but his body itself, or as here, fluid or secretions of his body. There seems to be no question that when such a specimen is given voluntarily the analysis thereof is admissible. The Court of Appeals therefore held that the evidence concerning the urinalysis was properly admitted in the trial court and that the judgment of the trial court be affirmed.—*Ridgell v. United States, 54 A. (2d) 679 (D. C., 1947).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

Annals of Surgery, Philadelphia

126:381-632 (Oct.) 1947. **Partial Index**

Address of President: Science and Humanism in Surgery. E. D. Churchill.—p. 381.

Gastro-Esophageal Resection and Total Gastrectomy in Treatment of Bleeding Varicose Veins in Banti's Syndrome. D. B. Phemister and Eleanor M. Humphreys.—p. 397.

Acute Cholecystitis Following Surgical Treatment of Unrelated Disease. F. Glenn.—p. 411.

Consideration of Pathologic Factors Influencing Five Year Survival in Radical Resection of Large Bowel and Rectum for Carcinoma. R. K. Gilchrist and V. C. David.—p. 421.

Adjuvants to Surgical Therapy in Large Bowel Malignancy. I. S. Ravdin, H. A. Zintel and Doris H. Bender.—p. 439.

Observations on Mortality from Acute Appendicitis at a University Hospital, 1916 to 1946. R. N. Schullinger.—p. 448.

*Studies upon Spinal Cord Injuries: I. Development of Automatic Micturition. J. Martin and L. Davis.—p. 472.

Control of Cancer. A. W. Oughterson.—p. 478.

The Specialty of Anesthesia and Its Application in Harvard University Massachusetts General Hospital Department. H. K. Beecher.—p. 486.

Graduate Training in Surgery in Veterans Administration Hospitals. C. B. Puestow.—p. 500.

*Toxoid Immunization in Experimental Gas Gangrene: Preliminary Report. W. A. Altemeier, W. L. Furste, W. R. Culbertson and others. —p. 509.

Pathophysiology of Cause of Death from Coronary Thrombosis. G. Murray.—p. 523.

*Factors Limiting Surgery for Essential Hypertension. P. Heinbecker. —p. 535.

Paradox of Aciduria in Presence of Alkalosis Caused by Hypochloremia. K. K. Van Slyke and E. I. Evans.—p. 545.

Essential Therapeutic Adjuvants in Surgical Arrest of Wolff-Israel Actinomycosis. M. Gage, C. Lyons and P. T. DeCamp.—p. 568.

Evaluation of Methods of Penicillin Therapy in Thoracic Surgery. J. H. Donnelly, F. J. Phillips, J. P. Bartlett and W. E. Adams. —p. 579.

Studies in Postoperative Convalescence. W. H. Cole, R. W. Keeton, N. O. Calloway and others.—p. 592.

Spinal Cord Injuries: Automatic Micturition.—The observations presented by Martin and Davis are based on an experience with 471 patients with injuries of the spinal cord. The establishment of efficient urinary function is one of the primary goals in the care of the patient with an injury of the spinal cord. Urinary function in the patients observed by Martin and Davis has appeared in one of the following five forms: (1) early return to normal micturition; (2) eventual return of partial voluntary control of micturition; (3) involuntary dribbling of urine, or the frequent uncontrolled passage of small amounts of urine; (4) absolute retention, a less common situation, and (5) automatic or reflex micturition. If complete normal urinary control or partial voluntary control aided by special efforts on the part of the patient to empty his bladder cannot be obtained, the ideal condition is that of automatic micturition. In numerous instances the authors have found proof of the efficacy of the indwelling catheter with tidal drainage not only in the establishment of automatic micturition but also as an aid in restoring partial voluntary control. In no case did automatic micturition develop while a suprapubic catheter was in place. On the contrary, many patients developed such urinary control following the removal of the suprapubic tube, placement of an indwelling catheter and training for a period of time thereafter with tidal drainage or with carefully controlled manual drainage. Automatic micturition will develop following a complete lesion at any level within the spinal cord or cauda equina. It does not appear in the presence of incomplete lesions of the cord. Cystometric examination at regular intervals will indicate when the catheter may be removed to allow the trial of automatic micturition, indicating that a reflex response to tension of the bladder wall is necessary for this activity. Automatic micturition will develop only when there is no mechanical obstruction of the neck of the bladder and when the sphincter is capable of reflex relaxation. Extravesical stimuli are an aid but not a necessity to the development and maintenance of automatic micturition. Automaticity will not develop in the patient with severe bladder sepsis, multiple calculi or severe debilitation.

Experimental Gas Gangrene: Preliminary Report.—Altemeier and his associates studied the possibilities of producing effective toxoid immunity against a severe form of experimental gas gangrene developed in the presence of crushed muscle and dirt in animals whose susceptibility and antigenic response are similar to those of human subjects. The studies were made on 364 guinea pigs, which were injected with Clostridium welchii toxoid and were then challenged at various intervals after the injection of the toxoid. The degree of protection was low in the early experiments, being 12 and 33 per cent, although blood antitoxin levels in excess of 0.1 unit per cubic centimeter were produced before challenge. When similar groups of animals were challenged with injections of toxin or bacterial culture into healthy muscle, 80 to 100 per cent of the animals were protected by blood levels in excess of 0.1 units per cubic centimeter. In subsequent experiments, however, modified procedures of immunization with toxoid have gradually increased the protection to 50 to 100 per cent of animals. The presence of an unknown factor or factors which contribute to the toxemia and mortality of experimental gas infection developing in the presence of crushed muscle and dirt is suggested by these studies. A high degree of immunity is possible by the injection of toxoid against gas gangrene produced by Cl. welchii, but the duration of the immunity is undetermined. Other studies are in progress to increase and extend the degree of immunity afforded by injections of Cl. welchii toxoid and to produce similar immunization with toxoids of the other clostridia associated with gas gangrene in anticipation of the development of an effective mixed toxoid for human prophylaxis against clinical gas gangrene.

Factors Limiting Surgery for Hypertension.—According to Heinbecker, the surgical treatment of essential hypertension has been based on the concept that it is due to overaction of the sympathetic nervous system. The increased activity of the sympathetic nervous system has been pictured as causing general or local vasoconstriction and an increased secretion of epinephrine. More recently such overaction has been regarded as responsible for the constriction of the renal blood vessels, thus leading to a release of renin. The author presents evidence that a humoral mechanism, not overaction of the sympathetic nervous system, is the primary cause of essential hypertension. It is postulated that in man hypophysial eosinophil cell overaction with a resultant trophic stimulation of the adrenal cortex as the result of functional depression of the hypothalamic nuclei innervating the neural hypophysis is the primary cause of essential hypertension. The only two organs capable of releasing humors concerned with the pathogenesis and symptomatology of hypertension and whose function can be modified by sympathectomy are the kidneys and the adrenals. Any beneficial effect to be obtained by removal of portions of the sympathetic nervous system in the treatment of essential hypertension is to be obtained when such removal results in a denervation of the adrenals and the kidneys. The removal of portions of the sympathetic nervous system more extensive than is required for denervation of the adrenals and the kidneys is unnecessary. The temporarily greater enlargement of the vascular bed effected by this means may cause a shunting of blood from the kidneys sufficient to impair their function and thereby, through the release of renin, accelerate the degenerative changes in the extrarenal blood vessels.

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Archives of Ophthalmology, Chicago

38:289-414 (Sept.) 1947

Correlations between Sensory and Motor Disturbances in Convergent Squint. F. H. Adler and F. Elizabeth Jackson.—p. 289.
Penicillin Therapy of Experimental Infections of Lens and Vitreous with Clostridium Welchii. L. C. Hoskins.—p. 301.
Lipemia Retinalis: Report of a Case. F. L. P. Koch and P. S. Strong. —p. 310.
Influence of Suture on Complications Following Cataract Operation. A. de Roetth.—p. 315.
*Ocular Involvement in Rats on Diets Deficient in Amino Acids: I. Tryptophan. A. Ferraro and L. Roizin.—p. 331.
*Id.: II. Corneal Dystrophy Due to Valine Deficiency. A. Ferraro, L. Roizin and I. Givner.—p. 342.
Cataract Complicating Glaucoma. G. Samuels.—p. 353.
Treatment of Subchoroidal Hemorrhage by Posterior Sclerotomy. P. A. Duehr and C. D. Hogenson.—p. 365.
Liability Test for Chronic Simple Glaucoma. S. Bloomfield.—p. 368.
Modified Snellen Suture for Prolapsed Chemosed Conjunctiva. J. Laval and J. Schneider.—p. 375.
Official Color Sense Control in Sweden. C. G. Boström and I. Kugelberg.—p. 378.

Ocular Involvement (I and II) in Rats on Deficient Diets.—Ferraro and his co-workers observed that most rats on tryptophan-deficient diets showed arrest of growth, loss of body weight, disappearance of the subcutaneous adipose tissue, alteration of fur, atrophy of the gonads and, at times, yellowish coloring of the incisor teeth with alteration of the enamel. Ocular changes in young animals included spectacle eyes, conjunctivitis, superficial vascularization of the cornea and occasionally cataractous changes in the lens. This group of animals did not live long on the deficient diet and generally died before presenting the more specific symptoms of tryptophan deficiency. In more mature rats spectacle eyes were apparent at times, but less frequently and to a lesser degree than in the younger group. However, corneal vascularization and, particularly, various degrees of cataractous changes in the lens were more constant. In adult rats, spectacle eyes and conjunctivitis were only occasionally noted, whereas vascularization of the cornea was more commonly observed. In rats maintained on a valine deficient diet the corneal changes seem to be the result of edema and progressive degeneration, leading gradually to keratinization and disorganization of the epithelial structure of the cornea. In addition, pronounced deep vascularization of the cornea is observed. Slight changes in the lens, characterized chiefly by vacuolation of the cortex, are only occasionally noted. These structural changes in the eye appear to be reversible (if treated in time), as demonstrated by notable improvement following the administration of synthetic valine to the animals on a valine deficient diet.

Archives of Otolaryngology, Chicago

46:269-426 (Sept.) 1947

Experience of Dizziness: Psychosomatic Observations on Some Vestibular Types. R. D. Loewenberg.—p. 269.
Speech Disorders in World War II: IX. Dysphonia. W. G. Peacher. —p. 282.
Role of Penicillin in Management of Acute and Chronic Frontal Sinusitis. K. M. Kahn.—p. 293.
Inhalation of Penicillin Aerosol and Penicillin-Streptomycin Aerosol in Office Practice. D. Davis.—p. 307.
Tonsil Problem. R. Waldapfel.—p. 318.
Nasal Sensitivity to Vasoconstrictors. R. W. Wright.—p. 330.
Microscopic Study of Inner Ear of Ataxic Rabbit. M. V. Anders. —p. 335.
*Melkersson's Syndrome: Report of 5 Cases, with Special Reference to Pathologic Observations. K. Kettel.—p. 341.
Relation of Various Fungi to Otomycosis. F. T. Wolf.—p. 361.
Otogenic Abscess of Contralateral Frontal Lobe: Report of Case. J. G. Waltner.—p. 375.
Endoscopic Use of Biplane Fluoroscope. E. W. Hagens.—p. 382.
Vestibular Apparatus as Organ of Sense. E. Wodak.—p. 386.
Anesthesia for Surgical Correction of Deafness. S. G. Hershey and M. F. Jones.—p. 390.
Tyrothricin in Treatment of Common Cold. D. Darling and C. F. Baumeister.—p. 395.

Melkersson's Syndrome.—Kettel reports 5 cases of Melkersson's syndrome in 2 young men aged 16 and 18 years respectively and in 3 women between the ages of 30 and 45. This syndrome comprises chronic swelling of the face, peripheral facial palsy, which may be bilateral and which may tend to relapse, and furrowed tongue. In all the patients the disease had its onset with facial palsy before the eighteenth year. In only 1 patient did the swelling of the face occur at the same time as the facial palsy; in the remaining 4 the paresis appeared from ten to nineteen years before the face became swollen. Some of the patients observed that the swelling began after they had been exposed to cold. In 3 of the patients the swelling was localized to the upper lip, in 2 to both the upper and the lower lip. Both clinically and pathologicoanatomically the facial palsy showed close correspondence to Bell's palsy. In 2 of the patients with bilateral palsy decompression of the facial nerve according to the Ballance-Duel method was done. While in the first patient nothing macroscopically abnormal could be demonstrated in the bone or the nerve on one side, extensive changes both of the mastoid process and the facial nerve were found on the other side. In the other patient there were no abnormal macroscopic findings in the cells of the mastoid process, the canal of the facial nerve or the nerve. During the chronic stage the swelling of the face is due to chronic edema which has all the characteristic features of angioneurotic edema. The facial palsy and the swelling of the face occur within the parts innervated by the facial nerve; it is suggested that in these patients this nerve, besides supplying the voluntary facial muscles with motor fibers, also conducts vasomotor fibers. Decreased function of the former results in facial palsy, whereas disturbance of the innervation of the latter causes neurotrophic facial edema.

Bulletin New York Academy of Medicine, New York

23:497-542 (Sept.) 1947

Tumors of Skeletal System: Pathologic Aspects. H. L. Jaffe.—p. 497.
Tumors of Skeletal System: Medical Aspects. A. B. Gutman.—p. 512.
Diagnostic Procedures in Investigation of Sterility in Female: Evaluation of Clinical Importance. I. C. Rubin.—p. 519.
Current Concepts of Fertility in the Male. R. S. Hotchkiss.—p. 533.

23:545-596 (Oct.) 1947

Harvey Cushing's Early Training 1887-1900. J. F. Fulton.—p. 545.
Causes of Cancer. L. Loeb.—p. 564.
Diseases of Collagen System. P. Klemperer. —p. 581.
Streptomycin Dosage Schedules for Clinical Use. L. Loewe and Erna Alture-Werber.—p. 589.

Journal of Immunology, Baltimore

57:101-202 (Oct.) 1947

Dilution Phenomenon in Titration of Antivenins (Antibothropic Sera). F. W. Eichbaum.—p. 101.
Studies on Reversibility of Antigen-Antibody Reaction: III. Relation Between Effects of Homologous Polysaccharide on Capsular Swelling and on Increased Aggregation of Sensitized Pneumococci. M. C. Morris and Helen V. Karr.—p. 115.
Interference Between Neurotropic and Other Unrelated Viruses. A. Vilches and G. K. Hirst.—p. 125.
Technic of Collodion Particle Agglutination. P. A. Cavelti.—p. 141.
Chemotherapeutic Effect of Acridine Compounds in Experimental Rickettsial Infections in Embryonated Eggs. J. E. Smadel, J. C. Snyder, Elizabeth B. Jackson and others.—p. 155.
Preparation of Highly Potent Endotoxin of Hemophilus Pertussis. J. Smolens and E. H. Flavell.—p. 173.
Isoallergic Encephalomyelitis and Radiculitis in Guinea Pigs After One Injection of Brain and Mycobacteria in Water-in-Oil Emulsion. J. Freund, E. R. Stern and T. M. Pisani.—p. 179.
Study of Influenza Virus Vaccines by a Serum-Virus Neutralization Test and by Active Immunization. Bernice E. Eddy.—p. 195.

Journal Industrial Hygiene & Toxicology, Baltimore

29:279-358 (Sept.) 1947

Studies on Toxicity of Inhaled Cadmium: I. Acute Toxicity of Cadmium Oxide by Inhalation. H. M. Barrett, D. A. Irwin and E. Semmons. —p. 279.
Id.: II. Acute Lethal Dose of Cadmium Oxide for Man. H. M. Barrett and B. Y. Card.—p. 286.
Id.: III. Pathology of Cadmium Smoke Poisoning in Man and in Experimental Animals. J. C. Paterson.—p. 294.
Effects and Treatment of Inhalation of Cadmium Chloride Aerosols in Dog. H. E. Harrison, H. Bunting, N. K. Ordway and W. S. Albrink. —p. 302.
Study of Industrial Exposures to Cadmium. F. Princi.—p. 315.
Possibility of Chronic Cadmium Poisoning. Harriet L. Hardy and J. B. Skinner.—p. 321.
Epidermal Application of Diethylene Glycol Monoethyl Ether (Carbitol) and Some Other Glycols: Absorption, Toxicity and Visceral Damage. P. J. Hanzlik, W. S. Lawrence, Jean K. Fellows, F. P. Luduena and G. L. Laqueur.—p. 325.
Lung Retention of Quartz Dust Smaller Than One Half Micron. T. F. Hatch and V. H. Kindsvatter.—p. 342.
Slow Dissolving, Nonirritating Salt Tablet for Use in Hot Environments. W. V. Consolazio, L. J. Pecora and T. Tusing.—p. 347.
Control of Lead Exposure in Storage Battery Manufacture. G. S. Winn and Carroll Shroyer.—p. 351.

Journal National Malaria Society, Columbia, S. C.

6:155-218 (Sept.) 1947

Laboratory Colonization of Anopheles Darlingi. M. Bates.—p. 155.
Laboratory Colony of Anopheles Darlingi. G. Giglioli.—p. 159.
Studies on Imported Malarias: 3. Laboratory Rearing of Western Anophelines. N. F. Hardman.—p. 165.
Practical Laboratory Methods for Quantity Rearing and Handling of Aedes Aegypti Mosquitoes to be Infected with Plasmodium Gallinaceum. H. A. Johnson.—p. 173.
Relative Effectiveness of Various Repellents Against Anopheles Farauti Laveran. B. V. Travis.—p. 180.
*Malaria Mortality and Morbidity in United States for Year 1945. E. C. Faust, J. A. Scott and G. E. McDaniel.—p. 184.
Automatic Siphons for Antimalarial Control of Tropical Streams. C. E. Newbold and E. Cochrane.—p. 192.
Medical Research in Malariology in First Postwar Year, 1945-1946; Report of Committee on Medical Research. H. Beckman.—p. 206.

Malaria in United States in 1945.—The report by Faust and his associates constitutes the sixteenth consecutive annual report to the National Malaria Society on the status of malaria in the United States. Practically all the reported military malaria was acquired overseas, and much of this is now widely distributed throughout the country as relapsing vivax infection in veterans who have been discharged from service. Malaria mortality in the civilian population continues to show a satisfactory decline. Within a decade it has been reduced approximately nine tenths. Yet there are areas of hyperendemicity remaining in the Southeastern states, in the Mississippi Valley, in eastern Oklahoma and Texas, and in the lower part of the Rio Grande Valley. Most reporting of malaria cases is still inadequate. Certain states, notably those in New England, New York, Ohio and Minnesota, all of which are regarded as essentially nonmalarious, now have widely disseminated cases of malaria in military or veteran personnel. Malaria in veterans in California is also considerable in volume. This may provide a means of reestablishing malaria in areas which have been essentially free of malaria for many years.

J. Neuropathology & Exper. Neurology, Baltimore

6:311-418 (Oct.) 1947

Histopathology of Thermocoagulation of Cerebral Cortex. M. L. Silver and A. E. Walker.—p. 311.
Hyperplasia of Peripheral Neuroglia a Factor in Pathologic Changes in Autonomic Ganglion Cells. A. Kuntz and N. M. Sulkin.—p. 323.
Pathology of Acute Disseminated Encephalomyelitis Produced Experimentally in Rhesus Monkey and Its Resemblance to Human Demyelinating Disease. A. Wolf, E. A. Kabat and Ada E. Bezer.—p. 333.
*Carcinoma of Muscle Tissue as Cause of Laryngeal Paralysis. G. B. Hassin.—p. 358.
*Sturge-Weber-Dimitri's Disease: Report of Abortive Case with Observations on Form, Chemical Nature and Pathogenesis of Cerebral Cortical Concretions. B. W. Lichtenstein and C. Rosenberg.—p. 369.
Essential Amino-Acid Deficiency, Clinicopathologic Findings in Rats: II. Valine. A. Ferraro and L. Roizin.—p. 383.
Perforated Duodenal Ulcer and Neoplasm of Tuber Cinereum in Newborn. J. I. Mossberger.—p. 391.
Experimental Contrast Radiography of Peripheral Nerves. J. D. French and W. H. Strain.—p. 401.

Carcinoma Causing Laryngeal Paralysis.—Hassin reports 1 case of bilateral paralysis of the recurrent laryngeal nerve caused by a large carcinoma in the upper third of the esophagus pressing on the trachea and also on the recurrent laryngeal nerves in a man aged 69. The patient became suddenly hoarse and experienced sharp shooting pains in the right side of the head. He died eleven weeks after the onset of the complaints. Necropsy revealed invasion of the muscle tissue by cancer cells, resulting in a variety of changes in the muscle fibers, namely, swelling, fragmentation, loss of striations, liquefaction, fibrillary disruption, degeneration and necrosis. No other pathologic condition of muscle exhibits such a wealth and combination of changes as demonstrated in a muscle invaded by carcinoma. Changes in the muscles and not in the nerves may have been the real cause of the paralysis. The degenerative changes exhibited by some muscle fibers were similar to those seen in progressive muscular atrophy and, like the other changes, are to be considered of toxic and not mechanical origin. Cancer of muscle fibers differs from that of nerve fibers in involving the parenchyma; in nerve fibers the cancer cells are confined to their mesodermal sheaths.

Sturge-Weber-Dimitri's Disease. — Lichtenstein and Rosenberg report 1 case of an abortive form of Sturge-Weber-Dimitri's disease (nevoid amentia), in which superficial hemangiomatous lesions were not demonstrable in a girl aged 15, who was classified as an idiot at the age of 7 years and who died from bacillary dysentery. The anatomic basis for Sturge-Weber-Dimitri's disease is hemangiomatous mesenchymal dysplasia in the cephalic region, the lesions being predominantly in the mesenchymal layer bordering on the ectoderm, namely, the subcutis, the submucosa of the mouth, nose and throat; the choroid coat of the eye, and the leptomeninx. In the authors' case necropsy revealed that the hemangiomatous lesions in the right occipital lobe were nests of telangiectatic veins which were engorged with blood, being limited to the overlying leptomeninx. The engorged telangiectatic veins played a part in producing venous and capillary stasis in the underlying cerebral cortex. This disturbance in circulation resulted in the depositions of concretions, which replaced large portions of the parenchyma. The concretions are generally rich in calcium or calcium admixed with iron, but in this case calcium was not found, the changes being exclusively in the nature of ferrugination rather than calcification. The concretions appeared histologically as isolated spherules, pericapillary sheaths and incrusted nerve cells. The sclerosis of the affected cerebral convolutions consisted of concretions and a diffuse increase in fibrillary glia, the latter being reactive to the concretions and secondary to the disappearance of nerve cells and the secondary degeneration of nerve fibers. These concretions appear in the roentgenogram as double contour lines outlining the cerebral convolutions. These double contour shadows seen in roentgenograms of the skull in cases of Sturge-Weber-Dimitri's disease are not specific for the disease and have been described in other disorders in which partial interference with the blood supply of the affected convolutions has occurred.

Journal of Neurophysiology, Springfield, Ill.

10:323-380 (Sept.) 1947

Potentials from Motor Roots of Crustacean Central Nervous System. C. A. G. Wiersma and W. Schallek.—p. 323.
Vestibular Nuclei as Excitatory Mechanism for Cord. L. M. N. Bach and H. W. Magoun.—p. 331.
Interpretation of Spinal Cord Action Potentials In Terms of Volume Conductor Theory. G. M. Schoepfle.—p. 339.
Study of Effects of Anesthesia and Asphyxia on Mono-Synaptic Pathway Through Spinal Cord. C. McC. Brooks and J. C. Eccles.—p. 349.
Electroencephalogram After Prolonged Brain Asphyxiation. A. van Harreveld.—p. 361.
Autonomic and Somatic Reactions Induced by Stimulation of Cingular Gyrus in Dogs. W. F. Kremer.—p. 371.

Journal of Nutrition, Philadelphia

34:351-469 (Oct.) 1947. **Partial Index**

Quality of Diet and Consumption of Sucrose Solutions. C. M. McCay and Eva M. Eaton.—p. 351.
*Comparative Biologic Availabilities of Ferrous Sulfate Iron and Ferric Orthophosphate Iron in Enriched Bread. H. Blumberg and A. Arnold.—p. 373.
Self Selection of Diet: V. Appetite for Carbohydrates. E. M. Scott and Ethel L. Verney.—p. 401.
Physiologic Availability of Vitamins: IX. Influence of Ascorbic Acid Stabilizers in Fruits and Vegetables. D. Melnick, M. Hochberg and B. L. Oser.—p. 409.
Studies of Thyroid Toxicity: I. Nutritional Factor Which Alleviates Toxicity of Ingested Thyroid Substance. J. J. Bethell, V. D. Wiebelhaus and H. A. Lardy.—p. 431.
Effect of Ingestion of High Levels of Riboflavin on Amount in Milk and Urine. P. B. Pearson and B. S. Schweigert.—p. 443.
Some Studies on Nutritive Value of Butter Fatty Acids. E. Heftmann.—p. 455.

Forms of Iron in Enriched Bread.—The biologic availability of the iron in ferrous sulfate and in ferric orthophosphate has been compared on the basis of hemoglobin regeneration in rats made anemic by iron deficiency. Comparison was made also with ferric chloride. The iron compounds were fed in the form of enriched breads, and multiple levels of enrichment with iron were used to permit comparison of dosage response curves. Under the conditions of these experiments Blumberg and Arnold found that the iron in ferrous sulfate was four to five times as available as that in ferric orthophosphate when both compounds were tested at four widely spaced levels. When compared at two levels, the iron in ferric chloride was equal in biologic availability to that in the highly effective ferrous sulfate or four to five times as available as the iron in ferric orthophos-

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phate. The authors stress the desirability of using highly assimilable forms of iron in the enrichment of flour and bread, so that the consumer may secure the full benefit of the enrichment program.

Journal of Thoracic Surgery, St. Louis

16:445-586 (Oct.) 1947

Specialism in Surgery. I. A. Bigger.—p. 445.
Lipoid Pneumonia Simulating Bronchogenic Carcinoma. R. M. Janes. —p. 451.
Gastrogenous Mediastinal Cyst. L. R. Davidson and L. Brown.—p. 458.
Mediastinal Enterocystoma: Report of Case in Seven-Month-Old Child with Impending Suffocation, Operation and Recovery. N. Lindquist and H. B. Wulff.—p. 468.
Treatment of Thoracogastric Fistula. G. E. Lindskog and E. A. Lawrence.—p. 477.
Congenital Eventration of Diaphragm. J. D. Bisgard.—p. 484.
*Pulmonary Function After Pneumonectomy and Lobectomy. G. Birath, C. Crafoord and P. Rudström.—p. 492.
*Tuberculous Tracheobronchitis: Study of 500 Consecutive Cases. A. R. Judd.—p. 512.
Should Solitary Pulmonary "Metastases" be Resected? P. W. Schafer and O. B. Scott.—p. 524.
Study of Variations of Bronchopulmonary Segments in Left Upper Lobe. J. G. Scannell.—p. 530.
Experience with Thoracic and Thoracoabdominal Wounds in an Evacuation Hospital. S. A. Mackler.—p. 538.
Traumatic Rupture of Bronchus. T. J. Kinsella and L. W. Johnsrud. —p. 571.

Pulmonary Function After Pneumonectomy. — Birath and his associates point out that pneumonectomies and lobectomies raise the question of whether the remaining lung tissue can carry on the respiratory function. The authors studied 12 patients who had undergone pneumonectomy and 14 patients who had undergone lobectomy for from two to thirteen years after the operation. They found that after pneumonectomy there is somewhat less reduction in total lung volume than the corresponding loss of parenchyma. In the position of maximum inspiration the remaining lung tissue (probably also in the lobectomy cases) is therefore exposed to increased distention. The distention of the lung tissue is approximately 50 per cent greater after pneumonectomy than has previously been calculated. The gaseous elements of the blood in the state of rest as a rule do not exhibit changes. After pneumonectomy and lobectomy, dyspnea is generally stationary and not progressive. After the postoperative period, it steadily diminishes. In many instances it is surprising how little the patient is troubled by it. Twenty-three of the 26 patients had full working capacity. If emphysema develops in the course of years, it generally remains within moderate limits and does not greatly encroach on respiratory function.

Tuberculous Tracheobronchitis.—Judd says that the routine endoscopic examination of all patients who are under consideration for major surgical collapse therapy for pulmonary tuberculosis has made it possible to accumulate much information regarding tuberculous endobronchitis and tracheitis. Among the facts that have been brought to attention are the progressive nature of the changes that culminate in a strangulating stenosis and the value of treatment. Observations were made in 500 cases. The majority of patients revealed some inflammatory reaction suggesting that the severer conditions have their origin in this inflammatory process, which may end in acute stenosis or total occlusion of the airway. The fact that every tuberculous patient does not suffer such a strangulating stenosis is proof that natural resistance interrupts this chain of events in the majority of cases. In addition, bronchoscopic management will interrupt many more. The ultimate number of patients in whom strangulating stenosis develops is small. Endoscopic methods can relieve and "cure" this type of lesion in many cases. Silver nitrate in from 5 to 30 per cent solution is easily applied to ulcerating and granulomatous areas. However, in some patients the application is followed by increase in tissue edema and inflammatory change. Fairly satisfactory results can be obtained by aspirating secretions, removing granulations with the gauze applicator and applying a soothing application, such as cajeput oil ("gomenol") or monochlorophenol in mineral oil. Only endoscopic examination will provide information about endotracheobronchial conditions. The author thinks that in time all patients with advanced tuberculosis will be bronchoscoped prior to the institution of collapse therapy.

Journal of Urology, Baltimore

58:221-294 (Oct.) 1947

Suprarenal Cortical Syndrome: Report of Case with Carcinoma of Adrenal Cortex. W. L. McLaughlin, J. P. Bowler and J. H. Folley. —p. 221.
Congenital Arteriovenous Aneurysm of Renal Artery. R. Pearse and R. L. MacMillan.—p. 235.
Anuria Following Blood Transfusion: Report of 2 Cases. N. E. Berry. —p. 239.
Transplantation of Ureters and Total Cystectomy. V. F. Marshall. —p. 244.
Artificial Sphincter: New Device and Operation for Control of Enuresis and Urinary Incontinence. F. E. B. Foley.—p. 250.
Acute Exudative Cystitis of Undetermined Etiology. J. V. Berry and N. E. Berry.—p. 260.
*Reiter's Syndrome: Report of 2 Cases with Response in 1 to Large Doses of Mapharsen. E. N. Khoury.—p. 268.
*Subacute Monocytic Leukemia Presenting Symptoms of Prostatism: Case Report. E. N. Lubin, T. R. Fetter and L. A. Erf.—p. 272.
Hematuria in Workmen in Aniline Dye Industry Due to 5-Chloro-Ortho-Toluidine: 6 Case Reports. J. S. Lyons.—p. 277.
*Glandular Metaplastic Malignancy in Urinary Tract: Report of 4 Cases. W. E. Kittredge, J. C. Henthorne and M. Whitehead.—p. 282.
Impotence Following Trauma to Corpora Cavernosa Relieved by Cartilage Grafts: Case Report. A. A. Solomon and C. I. Karleen.—p. 289.

"Mapharsen" in Reiter's Disease.—Khoury points out that Reiter's syndrome has a basic triad of abacterial urethritis, conjunctivitis and arthritis. The general belief is that it is one of the many virus infections. Cases reported in the literature generally had a protracted course, but this is not an invariable observation, inasmuch as at least 1 of the 2 cases reported here was benign and cleared in a comparatively short time. The second case may be classed as moderately severe. However, it did cause protracted disability. Large doses of oxophenarsine hydrochloride ("mapharsen"), which were started four months after onset of the urethritis, caused such a rapid and dramatic response that the possibility of a coincidental spontaneous regression cannot be rationally entertained. The author thinks that in future cases of this syndrome this form of therapy should have a trial. "Mapharsen" was given in two injections a week for three weeks, then one injection a week for four weeks. The dose was 0.06 Gm. administered by intravenous injection.

Monocytic Leukemia Appearing as Prostatism.—Lubin and his associates report the history of a man, aged 56, who was hospitalized with symptoms of prostatism. A persistent elevation of temperature and the abnormal blood picture prompted hematologic consultation, which resulted in a diagnosis of subacute monocytic leukemia. This is the second report of a case of monocytic leukemia in which the presenting symptoms were those of prostatic urinary obstruction. The repeated episodes of complete urinary retention can be explained on the basis of recurrent exacerbations of edema of the prostate secondary to the leukemic infiltration. The authors think that if transurethral electroresection is impractical in such cases, alleviation of the obstructive symptoms may be obtained by cystostomy.

Glandular Cancer of Urinary Tract.—Kittredge and his co-workers report 4 cases of glandular carcinoma of the urinary tract, which illustrate the difficulty of determining whether an adenocarcinoma is primary or secondary in this location. In 1 case the tumor of the bladder was probably metastatic from a carcinoma of the colon. In 2 cases the adenocarcinoma probably arose from plaques of urinary tract epithelium which had undergone metaplasia to the secretory type. In 1 case metaplasia of the epithelium to the secretory type evidently occurred in an infiltrating transitional cell carcinoma.

Northwest Medicine, Seattle

46:745-826 (Oct.) 1947

Pancreatic and Liver Function. A. J. Quick.—p. 762.
Differential Diagnosis of Jaundice. B. A. Brown.—p. 765.
Surgery of Pancreas. S. F. Herrmann.—p. 770.
Stricture of Extrahepatic Bile Ducts. W. W. Mattson.—p. 773.
Infectious Polyneuritis. G. A. Rickles.—p. 778.
*Acute Benadryl Poisoning. T. H. Duerfeldt.—p. 781.

Acute "Benadryl" Poisoning.—Duerfeldt describes the case of a girl 3 years of age, who swallowed approximately fourteen to sixteen capsules (700 to 800 mg.) of diphenhydramine hydrochloride ("benadryl hydrochloride"). The dose taken orally by this girl was 50 to 60 mg. per kilogram of body weight. The symptoms paralleled manifestations of a toxic dose in laboratory animals. At first the child walked with ataxic movements and

had twitching of the face and blurred speech. Suddenly she had generalized convulsive movements, stiffened out for a few seconds and then grew limp and gray and stopped breathing. With artificial respiration her color slowly returned, the muscular twitchings of the face appearing before normal respiratory movements began. Respiratory collapse occurred four times in less than four hours. The convulsions were finally brought under control with rectal administration of ether. The ataxia gradually decreased and disappeared after four days. Repeated examinations during the following months did not reveal evidence of damage to the brain.

Plastic & Reconstructive Surgery, Baltimore

2:297-402 (July) 1947

Total Ear Reconstruction: Preliminary Report. G. Aufricht.—p. 297.
Estlander-Abbe Operation in Treating Secondary Harelip Deformities and Defects of Upper Lip Resulting From Cancer. V. H. Kazanjian. —p. 307.
Surgical Treatment of Paralytic Stenosis of Larynx. L. H. Clerf. —p. 326.
Compressive Suspension Splint for Severely Comminuted Fractures. J. W. Maliniac.—p. 331.
Use of Open Jump Flaps in Lower Extremity Repairs. B. Cannon, C. E. Lischer, W. B. Davis and others.—p. 336.
*Successful Homologous Skin Grafting in a War Burn Using an Identical Twin as Donor. J. M. Converse and G. Duchet.—p. 342.
Method for Restoration of the Cilia of Eyelids. W. W. Schuessler and G. A. Filmer.—p. 345.
Blood Circulation in Pedicle Flaps: Preliminary Studies on a Photo-Electric Test for Determining Its Efficiency. B. Douglas and G. A. Millikan.—p. 348.
Useful Procedures in Plastic Surgery. G. W. Pierce, E. H. Klabunde and V. L. Bergeron.—p. 358.
Plastic Operative Procedure for Repair of Large Circular or Elliptical Body Surface Defects. B. Hadjistamoff.—p. 362.

Homologous Skin Grafting with Identical Twin as Donor.—Converse and Duchet point out that under the present status of knowledge it is impossible to assure homologous skin transplantation between individual human beings of ordinary genetic diversity. They describe the successful grafting of homologous skin in a case in which the patient's identical twin served as donor. The homografts were used to complete the covering of an area of full thickness skin loss following a war burn. The behavior of the homografts did not differ in any way from that of previously applied autografts. This case confirms previous reports on the success of skin grafting between identical twins.

Radiology, Syracuse, N. Y.

49:399-528 (Oct.) 1947

Clinical Diagnosis of Carcinoma of Cervix. A. N. Arneson.—p. 400.
Pathologic Aspects of Carcinoma of Cervix Uteri. W. J. Siebert. —p. 403.
Carcinoma of Cervix: Surgical Aspects. J. I. Brewer.—p. 404.
Intracavitary Radium Therapy for Carcinoma of Uterine Cervix. H. H. Bowing.—p. 406.
Interstitial Radium Therapy in Carcinoma of Cervix. G. W. Waterman. —p. 411.
Transvaginal Roentgen Therapy in Carcinoma of Cervix. J. A. del Regato.—p. 413.
Five-Year End-Results in Treatment of Carcinoma of Uterine Cervix. E. L. Jenkinson, E. L. Pirkey and F. J. Hamernik.—p. 415.
Improved Methods of Intravaginal Roentgen and Radium Therapy in Carcinoma of Cervix. E. C. Ernst.—p. 425.
Giant Cell Tumors of Bone. F. B. Bogart and A. E. Imler.—p. 432.
*Malignant Tumors of Small Intestine. H. P. Doub.—p. 441.
Further Observations with Intravaginal Roentgen Therapy of Cancer of Female Pelvis. W. W. Wasson and R. Greening.—p. 452.
Dosage Calculations for Various Plans of Intravaginal X-Ray Therapy. J. F. Nolan and W. Stanbro.—p. 462.
Diverticula of Foregut. D. Wheeler.—p. 476.
Medical, Biologic and Industrial Applications of Monochromatic Radiography and Microradiography. G. L. Clark.—p. 483.

Malignant Tumors of Small Intestine.—Doub says that although malignant tumors occur less frequently in the small intestine than in other parts of the gastrointestinal tract they are no longer considered as rare as they were in the past. In a review of observations in 52 cases he stresses that the highest percentage of malignant neoplasms of the small bowel are adenocarcinomas. Lymphosarcomas are second in numerical order and carcinoid tumors a poor third. Grossly, the tumors are of two types: constricting and fungating, or polypoid. The constricting type produces mechanical obstruction by narrowing the intestinal lumen; in the polypoid type obstruction is due to the bulk of the tumor or to intussusception. The clinical picture is usually one of a progressive loss of weight and strength and varying degrees of anemia. Pain is a prominent symptom. A change of bowel habit is usually present, and this may progress to an acute obstruction for which the patient seeks relief. A palpable tumor is an important and significant finding. Distention is often present. Unusual peristaltic activity is common. The roentgen picture may reveal an area of narrowing of the lumen of the bowel and dilatation proximal to it. Marginal or central filling defects may also be present, with obliteration of the mucosal markings in the involved area. Varying degrees of obstruction of the duodenum and stomach are commonly found associated with duodenal tumors. In the periampullary type jaundice, often of an intermittent character, is a prominent feature. The symptoms and roentgenologic signs of jejunal and ileal tumors are similar. In these areas the clinical syndrome is usually that of obstruction. The symptoms may be acute and constitutional in the case of intussusception or gradual in the case of a slow growing tumor. Loss of weight and strength combined with anemia and a palpable abdominal tumor are suggestive signs.

Urologic & Cutaneous Review, West Palm Beach, Fla.

51:559-620 (Oct.) 1947. **Partial Index**

Transurethral Management of Pathology of Female Urethra. S. H. Bassow.—p. 559.
Urinary Incontinence Due to Ectopic Ureteral Orifice with Cure by Heminephrectomy: Case Report. A. J. Greenberger, M. E. Greenberger and A. K. Swersie.—p. 563.
Supplementary Report on Combined Gyneco-Urologic Management of Vesicovaginal Fistula. W. J. Reich, J. L. Wilkey and M. J. Nechtow. —p. 566.
Complications of Endovesical Ureterotomy. R. Cowen.—p. 568.
*Ambulatory Intensive Treatment of Syphilis with Calcium Penicillin in Oil and Wax: Second Report. R. A. Koch.—p. 569.
Prostitution in Japan in Early Years of This Century. S. C. Martin. —p. 574.
*Marrow Aplasia and Estrapenia in Pemphigus Vulgaris: Case Report with Autopsy Findings and Notes on Relationship of Erythroid Marrow Function to Atopic-Exudative Skin Lesions. R. D. Barnard.—p. 586.

Calcium Penicillin in Syphilis.—Koch treated 279 patients with early syphilis by daily intramuscular injections of calcium penicillin in oil and 4.8 per cent beeswax for ten days at the San Francisco City Clinic during the period August 1945 to April 1947. Treatment consisted of two administrations of 150,000 units (0.5 cc.) of penicillin, one in the morning and one in the evening, making a total of 3,000,000 units of the drug for the entire treatment schedule. Of the 279 patients treated, 238 (85.3 per cent), 169 men and 69 women, completed the course of treatment. Thirty-five failed to complete the course for various reasons, and 6 of the patients are still under treatment. Eighteen patients displayed reactions, but in only 3 patients were these sufficiently severe to necessitate discontinuance of penicillin treatment. Of the 238 patients, 140 had primary syphilis and 98 had secondary syphilis. Sixty-eight of the 140 and 26 of the 98 attained seronegativity and were followed for periods varying from less than three months to more than eighteen months. One hundred and eighty-one of the 238 patients were followed from one to eighteen months. The failure rate of these cases was 10.5 per cent, and the failure rate based on 136 cases followed from three to eighteen months was 14 per cent. A combination of this method of treatment with arsenicals and bismuth compounds has been recommended for use in the physician's office.

Pemphigus Vulgaris.—Barnard reports 1 case of pemphigus vulgaris in a man aged 77; estrapenia, i. e., diminution in blood cholinesterase, and erythrophthisis were demonstrated at necropsy. It is suggested that the manifestations of pemphigus may be due to erythroid marrow depression, failure of cholinesterase synthesis and cholinergic intoxication. Fatal pemphigus may be classified along with the acute forms of malignant leukoses as an atopic exudative shock state. The bone marrow must be regarded as the crucial shock organ. On the basis of its presumed pathogenesis, blood transfusion appears to be the rational keystone in the treatment of pemphigus. Penicillin and arsenic therapy would appear to be useful. Radiation therapy may give the death blow to an erythroid marrow struggling for existence; this treatment is interdicted in all estrapenic conditions and would appear to be contraindicated in pemphigus.

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FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

22:129-192 (Sept.) 1947

Study of Burns and Scalds in Children. Brenda Morrison.—p. 129.
Excretion of 17-Ketosteroids and Gonadotrophin in Children: Normal and Abnormal Cases. A. M. Hain.—p. 152.
Medico-Social Problems Involved in Child Adoption. H. P. Tait.—p. 159.
*Absorption Collapse in Primary Tuberculous Infection in Childhood. S. Graham and J. H. Hutchison.—p. 162.

Absorption Collapse in Tuberculosis.—Graham and Hutchison show that drainage from the primary focus of tuberculosis takes place via the peribronchial lymphatics to the regional lymph nodes. Tuberculin skin tests are positive. A follow-up of positive reactors has revealed a varied course. By far the greatest number proceed to healing. Certain phenomena occasionally appear which are regarded as due to allergy, namely, erythema nodosum and phlyctenular conjunctivitis. Bronchogenic spread producing tuberculous bronchopneumonia and hematogenous spread producing miliary tuberculosis and tuberculous meningitis with rare exceptions end in death. The authors discuss the condition accompanied by extensive radiologic changes in the lungs which has been designated as epituberculosis. Various explanations have been attempted for this condition. The authors incline to the one which assumes that such lesions are due to the pressure of the tuberculous regional lymph nodes on the adjacent bronchi; the pressure produces various degrees of occlusion, which in turn leads to collapse of the corresponding lobe or sector (absorption collapse). Evidence in favor of this theory is presented. A number of illustrative case histories are given, and the authors stress that absorption collapse due to bronchial occlusion is of common occurrence in primary tuberculous infection in children. In some cases of incomplete bronchial occlusion, obstructive emphysema may result. The term "epituberculosis" applied to this condition is a misnomer, and the suggestion that the shadow seen in the radiograph indicates a perifocal reaction of an allergic nature is not justified. It might be suggested that in a child in whom a bronchus is occluded by a mass of tuberculous granulation tissue containing virulent tubercle bacilli bronchoscopy is contraindicated, and that the removal of the tuberculous granulation tissue via the bronchoscope might be followed by a rapid spread of the infection and the death of the patient. Such does not seem to be the case. Failure to bring about expansion of the collapsed lung may result in the development of bronchiectasis. Further observations on the final results obtained by bronchoscopy and removal of the obstruction compared with results in those not so treated are urgently required.

British Journal of Radiology, London

20:393-440 (Oct.) 1947

Developing Years of Physics in Medicine. S. Russ.—p. 393.
Micro-Arteriography. A. E. Barclay.—p. 394.
Optimal Skin Tolerance Dose Levels. B. Jolles and R. G. Mitchell.—p. 405.
Some Factors in Etiology of Osteochondritis of Spine: Report on 2 Families. F. H. Kemp and D. C. Wilson.—p. 410.
*Tomography of Spine in Tuberculous Disease. F. G. Wood and M. C. Wilkinson.—p. 418.
Radiologic Features of Vesical Leiomyoma and Leiomyosarcoma: Case Report. E. Samuel.—p. 423.
Two Cases of Lipomatosis Involving Bone. S. F. Oosthuizen and J. Barnetson.—p. 426.
Neuroepithelioma of Stomach. H. W. Gillespie.—p. 433.

Tomography in Tuberculosis of Spine.—According to Wood and Wilkinson, although ordinary anteroposterior and lateral radiographs are useful in defining the extent and progress of tuberculosis of the spine, there are situations in which such roentgen examination is made difficult by the intervention of structures that overlap and obscure the part to be viewed. Tomography is of special value in such regions. It is also of use in obtaining better definition of tuberculous foci in the spine. In 1 of the patients studied by the authors tomography made possible the accurate demonstration of the site of origin of the tuberculous sinus and the operative approach. In tuberculous paraplegia it is difficult to assess the integrity of the spinal canal by the ordinary anteroposterior and lateral films without the aid of tomographs. The authors cite cases and reproduce tomographs to show the value of tomography in the presence of tuberculous disease in the upper cervical, cervicodorsal and lumbosacral regions. They discuss tomography in relation to tuberculous paraplegia.

British Medical Journal, London

2:559-598 (Oct. 11) 1947

*Penicillin in Neurosyphilis. C. Worster-Drought.—p. 559.
Modern Treatment of Neurosyphilis. F. G. Lescher and H. R. M. Richards.—p. 565.
Primary Meningococcal Ophthalmia. F. N. Shuttleworth and J. G. Benstead.—p. 568.
Biochemistry of Senescence. C. P. Stewart.—p. 569.
Apparatus for Drainage of a Temporary Ileostomy. R. M. T. Walker-Brash.—p. 572.
Six Cases of Cardiovascular Disorder with Peripheral Neuritis. E. Leigh and A. R. Hazelton.—p. 573.

Penicillin in Neurosyphilis.—Worster-Drought employed sodium penicillin in aqueous solution. He thinks that a total dosage of at least 3,000,000 units of the drug should be given to patients with neurosyphilis and that in parenchymatous neurosyphilis the total dosage should reach 4,000,000 to 5,000,000 units. Intramuscular injection is the best method of administering penicillin. The intravenous route (either by continuous drip or by repeated single injections) has little to commend it. There is no evidence that the intrathecal administration of penicillin is of greater therapeutic value. Because of the reactions and the various additional risks, intrathecal injection of penicillin is best avoided in most cases of neurosyphilis. Owing to the risk of possible Herxheimer-Jarisch reactions following the first doses of penicillin, all patients with neurosyphilis should receive an initial series of injections of a bismuth compound. In meningovascular neurosyphilis the course of penicillin should be followed by arsenic and bismuth therapy. General paresis is best treated with an initial course of 4,000,000 to 5,000,000 units followed by full malarial or fever therapy (10 to 12 malarial rigors). The usual courses of arsenic and bismuth are advisable until the serologic reactions become negative. In cases of dementia paralytica (and taboparesis) in which malarial or fever therapy is contraindicated by reason of cardiovascular disease, one must rely on penicillin alone. Some improvement, but not cure, can be expected. Tabes dorsalis is best treated first with penicillin and then with arsenicals and bismuth preparations. In primary optic atrophy of syphilitic origin treatment should consist of an initial course of 4,000,000 to 5,000,000 units of penicillin followed by malarial therapy and afterward arsenic and bismuth therapy. Observation of patients must extend to five years or longer before success can be claimed for any treatment.

Journal of Laryngology and Otology, London

61:567-608 (Nov.) 1946

*Labyrinthine Fenestration—Present Position. C. A. Hutchinson.—p. 567.
Acute Otitis Externa in India. J. V. Clark.—p. 586.
Congenital Abnormalities of Pillars of Fauces and Action of Posterior Pillars and Nasopharyngeal Valve During Speech. M. C. Oldfield and I. P. J. Macnaughtan.—p. 594.
Considerations Regarding Secondary After Sensations Caused by Stimulation of Semicircular Canal System: Some Remarks on Paper of L. B. W. Jongkees and J. J. Groen. E. Wodak.—p. 601.
Hemorrhage from Internal Carotid Artery Following Pharyngeal Abcesses. E. C. Richardson.—p. 604.

Labyrinthine Fenestration.—Hutchinson favors the one stage posterosuperior operation under general anesthesia with gas-oxygen-trichloroethylene and with adoption of the operating microscope. Free and tangential access is provided by the posterosuperior approach in contrast to the vertical and restricted access afforded by Lempert's transmeatal approach. The actual fenestration itself is performed in a continuous controllable stream of isotonic sodium chloride solution to which a few drops of epinephrine have been added. The most suitable patient for operation is the young, intelligent adult between the ages of 20 and 30, with audiograms showing a flat conduction curve of more than 30 decibels and more or less good bone conduction hearing. Systematic treatment should be practiced both before and after surgical intervention. Vertigo may or may not occur;

its duration is usually short and the response to treatment with phenobarbital is satisfactory. The patient gets up about the sixth day and leaves the hospital about the twelfth to fourteenth day on the average. At the first dressing on the eighth postoperative day hearing may be as poor or poorer than it was before operation; about the end of another week it usually begins to improve, and it reaches its peak in two to six months. There is a fifty-fifty chance of a 25 to 35 decibel improvement in hearing, and such improvement if retained for two years will be permanent. The careful selection of cases, the thorough preliminary drilling of the theater team, the orthopedic preparation of the patient, a completely adequate armamentarium, the most rigidly aseptic operative and postoperative technic and meticulous attention to detail at operation are all factors of importance if success is to be attained. Since closure of the fenestration as the result of osteogenesis may occur up to two years from the date of operation in some 10 per cent of cases regardless of what steps are taken to prevent it, this period of time should be allowed to elapse in every instance before attempting to assess the permanent degree of success.

Journal of Pathology and Bacteriology, Edinburgh

59:1-358 (Jan.-April) 1947. **Partial Index**

Atypical Amyloidosis in Case of Plasma-Cell Myelomatosis. J. H. Fodden.—p. 29.
Behavior of Salmonella Typhi in Agglutination Reaction. W. Hayes.—p. 51.
Activation of Hemagglutinins by Human Serum. Kathleen E. Boorman and Barbara E. Dodd.—p. 95.
On Certain Properties of Antisera Prepared Against Human Serum and Its Various Protein Fractions: Their Use in Detection of Sensitization of Human Red Cells with "Incomplete" Rh Antibody, and on Nature of This Antibody. R. R. A. Coombs and A. E. Mourant.—p. 105.
Penicillin and B. Anthracis. J. M. Barnes.—p. 113.
Carcinoma of Pituitary Gland with Metastases to Liver in a Case of Cushing's Syndrome. W. Forbes.—p. 137.
Hemolytic Activity of C. Diphtheriae. L. F. Hewitt.—p. 145.
Effect of Asbestos on Tissue Cultures: Comparative Study with Quartz and Coal Dust. T. H. Belt, I. Friedmann and E. J. King.—p. 159.
Immunologic Aspects of Experimental Haemophilus Pertussis Infection. H. Proom.—p. 165.
Case of Idiopathic Methemoglobinemia Treated by Ascorbic Acid and Methylene Blue. E. J. King, J. C. White and M. Gilchrist.—p. 181.
Isolation and Cultivation of Variola Virus on Chorio-Allantois of Chick Embryos. A. W. Downie and K. R. Dumbell.—p. 189.
Cytoplasmic Basophilia of Bone Marrow Cells. J. C. White.—p. 223.
*Sensitivity of Organisms of Genus Leptospira to Penicillin and Streptomycin. J. A. H. Wylie and E. Vincent.—p. 247.
Some Characters of Coagulation Necrosis Due to Mustard Gas. B. D. Pullinger.—p. 255.
Adrenal Tumors and Pseudo-Hermaphroditism: Hormone Study of Cases. A. M. Hain.—p. 267.

Sensitivity of Leptospirae to Penicillin and Streptomycin.—Wylie and Vincent tested twenty-nine strains of leptospirae in vitro against penicillin and streptomycin. In the concentrations tested both antibodies partially or completely inhibited all the strains; there was considerable variation in susceptibility between species, but most of the common pathogens were completely inhibited by 0.5 unit per cubic centimeter or less. Strain variation in resistance was shown within the species Leptospira icterohemorrhagiae. On the whole, on a weight basis, penicillin was more inhibitory than streptomycin.

Lancet, London

2:531-566 (Oct. 11) 1947

Social Class and Fetal Mortality. D. Baird.—p. 531.
Hypoglycemia Following Partial Gastrectomy: Report of 3 Cases. C. G. Barnes.—p. 536.
Tuberculous Rheumatism: Report of Case. R. J. T. Woodland.—p. 540.
*Effect of Beta-Chloroethylamine Hydrochlorides in Leukemia, Hodgkin's Disease, and Polycythemia Vera: Report on 18 Cases. J. F. Wilkinson and F. Fletcher.—p. 540.
*Rhesus Antigen C^w Causing Hemolytic Disease of Newborn. Sylvia D. Lawler and J. J. van Loghem.—p. 545.

Beta Chloroethylamine Hydrochlorides in Leukemia.—Wilkinson and Fletcher describe the results of treatment with intravenous halogenated alkylamine (nitrogen mustard) in 18 cases of chronic myeloid and lymphatic leukemia, Hodgkin's disease and polycythemia vera. Diagnosis was confirmed by biopsy of lymph nodes or of sternal marrow. The most beneficial effects were observed in chronic myeloid leukemia, though dramatic improvement also occurred in Hodgkin's disease. There was considerable variation in the response to treatment in individual cases in all groups, but the least satisfactory results were obtained in chronic lymphatic leukemia. A dosage of 0.1 to 0.2 mg. per kilogram of body weight was adopted, and *tris* (beta-chloroethyl)amine hydrochloride was the compound of choice. Undesirable toxic effects were avoided by hematologic control and a safe technic of administration. The two alkylamines do not appear to cure leukemia or the other conditions mentioned, but in some cases they give relief by reducing the total white blood cell count, with a resultant improvement in the anemia. In other cases embarrassing enlargements of the lymph nodes, liver and spleen disappear, leading to an increased feeling of well-being. Improvement is seldom maintained, and the patient's response to this treatment appears to diminish after repeated injections. It may be an advantage to use some form of combined therapy or to give different preparations of varying activity on the hemopoietic organs at certain stages of the disease.

Rhesus Antigen C^w and Hemolytic Disease of the Newborn.—Lawler and van Loghem point out that a rare Rh antigen, C^w was described by Callender and Race in 1946. A patient responded to blood transfusions by making a succession of "new" antibodies. One of these antibodies was called anti-C^w. Two of the donors were eventually recognized as being C^wDe/CDe. C^w is a form of antigen alternative to C or c; it occurs in the bloods of about 2.5 per cent of English persons. The authors report a second example of anti-C^w. In this case the Rh antibody, anti-C^w, resulted from immunization by pregnancy and caused hemolytic disease of the newborn. The mother had never received a transfusion, but her first child had been jaundiced for a month. It recovered, however. A second infant died on the third day from icterus gravis. A year later a macerated fetus was stillborn. This was followed by a miscarriage during the fourth month. Another infant died from icterus gravis neonatorum, and the last infant, born in June 1947, died of erythroblastosis fetalis. The mother's serum, taken after the birth of the last child, agglutinated the cells of both father and baby. The blood groups of the family at first appeared to be compatible in all respects. Nevertheless the presence of the antibody and the history, which was typical of hemolytic disease, strongly suggested that Rh incompatibility must be present. The samples of blood from both mother and father were then tested against the serum of the Oxford patient containing the original anti-C^w agglutinin. The antigen C^w was found in the father's blood but not in the mother's; thus an Rh antigen incompatibility was disclosed. The antibody in the mother's serum was then proved to be anti-C^w by testing its reactions with a panel of cells of laboratory workers previously tested with the Oxford serum.

Medical Journal of Australia, Sydney

2:349-380 (Sept. 20) 1947

Management of Hand Injuries. F. H. McC. Callow.—p. 349.
*Management of Hand Injuries, Especially Treatment of Injuries to Bones and Joints. L. J. Woodland.—p. 351.
Pelvic Inflammation. R. F. Matters.—p. 354.
Infection with Salmonella Glegdam Amongst Natives of New Guinea: Account of 14 Cases with Post-Mortem Reports of 4 Fatal Cases. H. I. Jones and F. Fenner.—p. 356.

Management of Hand Injuries.—Woodland pleads for recognition of the seriousness of injuries to the hand and digits. Mangled fingers and hands result in more permanent deformities than major fractures of the large bones, and injuries to the hand and fingers result in far greater economic loss to the patient. The annual report of the Workers' Compensation Commission of New South Wales for the year 1944-1945 shows that there were 86,906 cases of compensated injury. Of these injuries, 26,862 (31 per cent) involved either the digits or the hand. After analyzing the location and nature of hand injuries, the author discusses the 2 commonest injuries of bones and joints of digits, fracture of the index finger and sprains of the thumb. Sepsis of the hand and treatment of stiff fingers is also discussed. He stresses that in addition to the uniform adoption of the improved technic in the treatment of fracture of bone and joints of the hands, more hospital beds and facilities for remedial occupational therapy in workshops are necessary before the disability rate will be lowered.

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Acta Chirurgica Scandinavica, Stockholm

96:1-96 (Sept. 10) 1947

Solitary Neurinoma of Small Intestine. W. Möller.—p. 1.
Intrathoracic Gastric Cyst. J. C. Christoffersen.—p. 12.
*Surgical Aspect of Acute Hepatitis. E. Bergefeldt.—p. 17.
Anorectal Malignant Melanomas: Clinical Study Based on 2 Cases. O. Müller.—p. 39.
*Value of Postoperative "Dicumarol" Prophylaxis at "Early Rising." S. Borgström.—p. 47.
*Appendicitis Material at Karolinska Sjukhuset 1940 to 1944. T. Ekström. —p. 62.
Clinical Significance of Study of Supraclavicular Lymph Nodes in Cancer. E. Jakobson.—p. 75.
Two Cases of Primary Suppurative Psoas Myositis. E. E. Vuori.—p. 87.

Acute Hepatitis.—Bergenfeldt operated on 7 patients with acute hepatitis, 4 men and 3 women between the ages of 42 and 58, in whom jaundice was refractory to medical treatment. Surgical intervention consisted of perfusion of the biliary passages with contrast medium for cholangiography supplemented by perfusion with isotonic sodium chloride solution in certain cases. The jaundice disappeared rapidly and the patients recovered. Relapses did not occur, and all the patients were in good health on follow-up examination up to three years and nine months after the operation. It is suggested that a relative obstruction was caused in the lower part of the common bile duct by an accumulation of tenacious mucus and cohesion of the mucosal surfaces. The hepatitis is accentuated by the impeded flow of bile, which is under subnormal pressure due to the hepatitis; the pressure drops still further, and a vicious circle develops. This is broken by the surgical intervention. The relative obstruction of the common bile duct must be considered not as the cause but as the result and complication of the hepatitis. The biliary passages of a patient who died of acute hepatitis were perfused during necropsy; a firm plug of mucus was expelled from the duodenal papilla, followed by large quantities of mucus. Similar observations were made in the postmortem of a pig which had died of acute hepatitis. The results of the serum citric acid test and the serum phosphatase test also support the author's concept. Surgical treatment is recommended in doubtful cases in which differential diagnosis of hepatitis from obstructive icterus may be difficult and in certain cases of hepatitis in which severe icterus has persisted for weeks or months. Surgical intervention should consist in cleansing the biliary passages; this may be achieved by perfusion.

Postoperative "Dicumarol" Prophylaxis.—Borgström divided 1,831 patients, 900 men and 931 women between the ages of 25 and 85 years, who were operated on at the surgical clinic in Lund during 1946, into two groups. Nine hundred and forty patients with odd numbers were to be given "dicumarol" therapy provided that this was not contraindicated, while 891 patients with even numbers were to serve as controls, being treated only by early ambulation. Only 701 (337 men and 364 women) of the 940 patients were treated with "dicumarol" while 1,130 (563 men and 567 women) were not. These two groups were comparable as to age, operative intervention, time in bed postoperatively and weight. The two latter factors were examined only in patients operated on for appendicitis, hernia and cholelithiasis. Patients with transvesical prostatectomy have not been included because of their greater age (68 at an average) and the high incidence of thromboembolism among these patients. By dividing the material according to sex, no difference was observed in the incidence of thromboembolism among the men treated with "dicumarol" and those of the control group, while the incidence of thromboembolism was definitely lower among the women treated with "dicumarol" and those not so treated. This applies to the statistics based on the whole group of 940 patients compared to those based on the 701 patients. In addition it was demonstrated that the risk of bleeding associated with postoperative "dicumarol" therapy is insignificant and that the incidence of fatal pulmonary embolism has been definitely reduced. Postoperative "dicumarol" prophylaxis is suggested for women at postoperative early rising, while for men this prophylaxis seems to be without demonstrated value. A possible decrease in the incidence of fatal pulmonary embolism should, however, be emphasized.

Appendicitis.—Ekström reports 2,349 cases of appendicitis in 1,654 men and 695 women. The mortality for the whole group was 0.38 per cent ± 0.01 per cent. Sixteen hundred and four of these patients were operated on for acute appendicitis. The percentage of perforations (7.4) was unusually low and may be related to the fact that the patients came from a large urban population and had been admitted to the hospital early after the onset. This may also account for the low mortality of 0.44 per cent ± 0.16 per cent in this group. Postoperative chemotherapy may have played an additional part. Temperature, blood sedimentation rate and white blood cell count were of secondary aid to diagnosis. Nineteen of 33 patients with appendical abscess were operated on; treatment consisted of drainage in 17 and of appendectomy in 2. Conservative treatment was practiced in the others, for whom an appendectomy was advised at a later time. Death resulted from cardiac decompensation in 1 patient aged 73. Four hundred and forty-nine patients with noninflamed appendixes were operated on because of diagnosis of acute appendicitis. The commonest cause of the erroneous diagnosis was intestinal infection of various types Women were in a significant majority (68 per cent), perhaps because intestinal disturbances are more frequent among women. One death occurred in this group, but it was not related to the operation. Two hundred and sixty-three patients with chronic appendicitis underwent operative intervention. Four-fifths of the patients were women. In 20 per cent the appendix was normal. Follow-up studies showed that 187 (83 per cent) were completely free from all abdominal symptoms. The best results were obtained in the cases of active chronic inflammation of the appendix and in cases with a typical history; in this group no deaths occurred among those who submitted to operation.

Acta Medica Scandinavica, Stockholm

128:509-603 (Sept. 22) 1947. **Partial Index**

*Treatment of Postdiphtheritic Polyneuritis with Vitamin B_1. J. Bøe. —p. 509.
*Examination of "Diodrast" Clearance and Tubular Excretory Capacity in Man by Means of Two Single Injections of "Diodrast" (Umbradil). B. Josephson.—p. 515.
Boeck's Sarcoid with Erythema Nodosum as an Initial Symptom: Report of a Case. C. J. Bjerkelund.—p. 538.
Pathophysiologic and Clinical Aspects of Crises of Asthma Bronchiale: I. Pulmonary Ventilation, Oxygen Uptake and Blood Pressure. H. Colldahl.—p. 551.
Concept of Renal Thresholds. J. A. Barclay, W. T. Cooke and R. A. Kenney.—p. 578.
Bilateral Pneumothorax in Cases of Diphtheria in Which Tracheotomy Was Performed. J. Bok and J. B. Mullers.—p. 584.

Vitamin B_1 in Postdiphtheritic Polyneuritis.—Bøe points out that since vitamin B_1 has given excellent results in the polyneuritis of beriberi it has also been tried in other forms of polyneuritis, although in these the indications for its use are not so definite. In the course of an epidemic of diphtheria with many toxic cases, an investigation was undertaken to ascertain the extent to which thiamine can prevent polyneuritis and whether large doses of this vitamin, given when polyneuritis had appeared, could have any influence on the course of the disease. Of 80 patients with toxic diphtheria every other one was treated with thiamine, the alternate patients serving as controls. The patients receiving vitamin B_1 were given 3 mg. daily by mouth, and as soon as signs of polyneuritis appeared they received a supplementary dose of 25 mg. of vitamin B_1 given daily by injection for five days. After ten days without therapy a new series of five injections of 25 mg. each was given. These injections for five days with ten day intervals were repeated as long as the patient remained in hospital. With this dosage vitamin B_1 appeared to have no effect whatever on the polyneuritis. Complications appeared just as often, just as early, and lasted just as long in the vitamin treated group as in the control group. There would seem to be little evidence in support of the employment of vitamin B_1 in postdiphtheritic polyneuritis.

"Diodrast" Clearance and Tubular Excretory Capacity.—Josephson reviews several technics of determination of renal "diodrast" clearance and of renal tubular excretory capacity for "diodrast" (iodopyracet injection U. S. P.), pointing out their shortcomings. Since 1942 he used a method, which he found comparatively convenient and reliable, consisting of a combina-

tion of two injections for the determination of renal plasma flow and tubular excretory capacity. The "diodrast" clearance is studied after one single intragluteal injection of the contrast medium and the tubular excretion capacity after one subsequent single intravenous injection.

Archivio Italiano di Chirurgia, Bologna

69:171-238 (Fasc. III) 1947. **Partial Index**

*Tuberculosis of Thyroid: 2 Cases. G. Coggi.—p. 223.

Tuberculosis of Thyroid.—The condition is rare. The subjects of Goggi's report are 2 women aged 26 and 58 years, respectively. The youngest patient had healed pulmonary tuberculosis. A cold abscess developed within a thyroid adenoma secondary to healed pulmonary disease. Treatment consisted of partial thyroidectomy. The older patient was suffering with tuberculosis of the tibia and of the tarsal bones. Thyroidectomy was contraindicated because of the acute degree of infiltration of the perithyroid tissue. Treatment consisted of transfission of the thyroid tumor and use of filiform drains for two months. In both cases the diagnosis of tuberculosis of the thyroid was verified by histologic studies of the removed tissue and biologic tests.

Bruxelles-Médical, Brussels

27:2265-2322 (Oct. 19) 1947

Role of Physical Therapy in Infections of Hand. P. Bauwens.—p. 2275.
*Antithyroid Action of Estrone. J. Lederer.—p. 2290.

Antithyroid Action of Estrone.—According to Lederer, goiter is much more frequent in women than in men, the ratio being about 9:1. Numerous studies have revealed a close functional relation between thyroid and ovary. Goiter and hyperthyroidism often occur following decisive changes in the genital sphere of women, at the time of puberty, pregnancy, menopause and castration. Accordingly, it was decided to try estrone in the treatment of those cases of hyperthyroidism that were associated with suppression of the ovarian function. The author presents the histories of 4 women with exophthalmic goiter in whom large doses of estrone were given. In 2 of them the hyperthyroid condition developed following castration and in 2 others during the menopause. In those who had undergone castration, 25 mg. of estradiol benzoate was injected during the first week; during the succeeding two weeks 20 mg., and after that 15, 10 and 5 mg. of the drug were injected weekly. The women of menopausal age at first were given two weekly intramuscular injections of 5 mg. of estradiol benzoate; then this dose was given once every week and finally once in two weeks. As a result of this treatment the patients improved rapidly. They gained in weight, the basal metabolic rate and the pulse rate decreased, the goiter diminished considerably and the exophthalmos regressed.

Chirurg, Würzburg

17/18:1-48 (Oct.) 1946. **Partial Index**

Essential Simplification of "Plastic of Perthes" in Paralysis of Radial Nerve. K. H. Bauer.—p. 1.
Safe Closure of Aboral Stump of Stomach in Finsterer's Excision for Exclusion. O. Kleinschmidt.—p. 6.
Physiology of Muscle Applied to Bone Fracture, Its Healing and Treatment. E. Rehn.—p. 14.
"Ventrifixation-Disease." H. H. Schmid.—p. 19.
Internal Anastomosis in Treatment of Cyst of Pancreas. E. König.—p. 24.
*Successful Treatment of Severe Air Embolism by Puncture of Ventricle of Heart. W. Lembcke.—p. 31.

Severe Air Embolism.—Lembcke reports 1 case of severe air embolism which occurred during skin suture after strumectomy in a woman aged 33. The clinical aspect resembled that of asphyxia. The patient was unconscious, the pupils did not react, the reflexes were absent. Peroral intubation demonstrated that the air passages were free. Circulatory and respiratory analeptics were ineffective, and only temporary improvement in the cadaverous discoloration of the skin resulted from the administration of oxygen. The presence of bloody foam was revealed by puncture of the right ventricle by means of a thin cannula. The foam was sucked off with an airtight syringe. The puncture was repeated three times. The first punctures resulted in only temporary improvement of circulation and respiration, and the patient remained unconscious. The third time the cannula was left in the right ventricle for ten minutes and air and foam were sucked off repeatedly. The pupils began to react, the pulse became less rapid, the cadaverous color of the skin changed to mild cyanosis and consciousness was restored in twenty minutes. It is suggested that the air embolism resulted primarily from disturbance of the air exchange depending on an obstruction of the blood current between the right heart and the capillaries of the lungs. The right ventricle, the pulmonary artery and part of the capillaries of the lung were obstructed by the air that had entered the circulation. Small amounts of blood still reached the lungs, but the blood supply of the various organs was insufficient, thus causing a severe decrease in function. The heart which is filled with air beats "in vain." This combined with the insufficient supply of blood to the heart and the organs would result in the cessation of the circulation. The only effective method of treatment is the removal of the mechanical obstruction of the right heart by sucking off the air. This measure may then be followed by the administration of various analeptics.

Gynaecologia, Basel

124:65-128 (Aug.) 1947

*Significance of Porphyrinuria for Diagnosis of Extrauterine Pregnancy. W. Neuweiler and Julia Rupp-Haller.—p. 65.
Duration of Pregnancy and Weight of the Newborn During the Starvation Period of 1944-1945 in Holland. J. A. Stroink.—p. 78.
Perforations at the Women's Clinic of the University of Szeged from 1921 to 1945. K. Magyar.—p. 85.
Tocodynamometer, Instrument for Measuring Uterine Contractions: Its Use in Obstetric Practice. S. Lóránd.—p. 98.
Indications, Technic and Results of Penicillin Therapy in Infections of Obstetric Origin. M. Mayer.—p. 105.

Porphyrinuria in Extrauterine Pregnancy.—Neuweiler and Rupp-Haller report that at the Women's Clinic of the University of Bern the porphyrin content of the urine was determined in nearly 400 patients in whom extrauterine pregnancy was present or suspected or who had other disorders in which porphyrin excretion was of interest. Porphyrin was demonstrated by means of the rapid method of Brugsch, which is based on the red fluorescence of the porphyrins in ultraviolet light. In two thirds of 122 patients with extrauterine pregnancy the porphyrin excretion in the urine was noticeably or considerably increased. In nearly a fifth the porphyrin reaction was weak, and in the remaining patients porphyrinuria was absent. Considering separately the various forms of extrauterine pregnancy, the authors found that in case of interrupted extrauterine pregnancy with the formation of hematocele, the incidence of porphyrinuria was somewhat higher; it occurred in 18 of 21 patients. As a rule, the porphyrinuria appeared rapidly, that is, from one to two days after onset of intra-abdominal hemorrhage. The authors found that porphyrinuria was a much more reliable indication of intra-abdominal hemorrhage than the urobilinogenuria. Of 100 women with intrauterine abortion, 28 had a greatly increased and 12 a weak elimination of porphyrin and in the other 60 it was normal. In patients with adnexitis porphyrinuria was positive in 58 per cent and negative in 42 per cent. In patients who had ovarian tumors with torsion of the pedicle and usually with hemorrhagic perfusion, 13 of 17 showed a great increase and 2 a slight increase in urinary porphyrin.

Klinische Wochenschrift, Würzburg

24/25:1-64 (Oct. 1 and Oct. 15) 1946. **Partial Index**

Physiologic Bases of Mechanics of Heart. H. Reichel.—p. 1.
*Enterococcic Pneumonia: Contribution to Problem of Chemoresistant Pneumonia. H. Lüdin.—p. 8.
Comparative Study on Effect of Some Sulfone and Sulfonamide Compounds on Streptococci in Vivo and in Vitro. W. H. Wagner and J. Kimmig.—p. 12.
Pathogenesis of Field Nephritis. K. Voit.—p. 14.
Carbohydrate Metabolism in Experimental Traumatic Tetanus. H. Staudinger.—p. 16.
*Oral Treatment of Pernicious Anemia with Small Amounts of Liver. F. Bahner.—p. 28.

Enterococcic Pneumonia.—Lüdin reports 7 cases of enterococcic pneumonia in 4 women and 3 men between the ages of 25 and 63. The patients had severe bronchopneumonia which was resistant to sulfonamide compounds. Bacteriologic studies revealed enterococci in the sputum; pneumococci were absent. In 1 patient a drop in temperature, rapid improvement in the general condition and lowered pulse rate followed the administration of antienterococcus monovalent horse serum. Fifteen

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cubic centimeters of the serum were given by intramuscular route and 10 cc. intravenously. A second intravenous injection of 20 cc. was given the next day. Enterococci may be considered as an etiologic factor in pneumonia even though they have been found in the oral and pharyngeal cavities and in about 20 per cent of sputums of normal persons and have been described as nonpathogenic for man.

Liver Treatment of Pernicious Anemia.—Bahner treated 15 patients with pernicious anemia by oral administration of small amounts of predigested beef liver. The initial daily dose consisted of 20 Gm. of cut liver mixed with acid gastric juice. An approximate ten week course of treatment was required for restoring the blood picture to normal. Twenty grams of predigested liver twice a week were required as a maintenance dose in 7 patients, 20 Gm. of predigested liver three times a week in 2 patients and 20 Gm. of predigested liver six times a week in 6 patients. Additional treatment consisted of 1 teaspoon of hydrochloric acid in 1 glass of water at each meal. In recent cases of pernicious anemia routine treatment has now been instituted with daily doses of 40 Gm. of predigested liver to be continued until the blood picture has been restored to normal, after which a maintenance dose of 20 Gm. of predigested liver several times a week may be sufficient. To cure pernicious anemia the maintenance dose should be increased to 40 Gm. daily. There were no failures. The advantage of beef liver administered by mouth, as compared to liver extract administered intravenously, consists in the richer content of vitamins and highly potent proteins. This is particularly important in countries where nutrition is precarious, because administration of antipernicious substance leads to renovation of blood only provided that the erythropoietic apparatus has enough food proteins at its disposal. By the method described pernicious anemia can be cured in ambulant patients independently of liver extract preparations. Combined parenteral and oral treatment is indicated if there are only limited quantities of liver extract preparations available or if the available preparations are not adequately effective.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

91:2637-2716 (Sept. 20) 1947. **Partial Index**

*Generalized Necrotizing Arteritis Following Use of Sulfonamides. T. C. van Rijssel and L. Meyler.—p. 2649.
Spondylarthritis Ankylopoietica (Bechterew's Disease): Treatment. D. L. Hulst.—p. 2658.
Improved Method of Search for Treponemas in the Dark Field. A. Bijdendijk.—p. 2667.

Necrotic Arteritis Following Sulfonamide Therapy.—Van Rijssel and Meyler report 6 patients in whom necropsy revealed necrotizing arteritis, which was attributed to allergy resulting from medication with sulfonamide compounds. In view of the serious dangers resulting from sensitization, the authors issue a warning against the use of sulfonamide drugs in cases in which they are not strictly indicated. The authors cite the case of a patient with carcinoma, who was given large doses of sulfadiazine in treatment of pneumonia. He died, and necropsy revealed arteritis in spleen, liver and lungs. The renal vessels were not involved, and the clinical history indicates that the renal function had been unimpaired to the end. This indicates that arteritis may develop in sulfonamide therapy even when the function remains normal.

Ophthalmologica, Basel

114:129-192 (Sept.) 1947. **Partial Index**

*Chronic Superficial Punctate Keratitis by Onchocerca Volvulus. M. Appelmans.—p. 129.
Action of Testosterone Preparations on Intraocular Pressure. Magda Radnót.—p. 168.

Chronic Superficial Punctate Keratitis by Onchocerca Volvulus.—According to Appelmans the chronic form of punctate keratitis prevails in endemic form in central America and in tropical Africa. Its etiologic basis is variable. They report 2 cases in which chronic superficial punctate keratitis was caused by Onchocerca volvulus. The patients were Europeans recently returned from the Belgian Congo. A definite diagnosis of onchocerciasis requires the biomicroscopic demonstration of mobile larvae. It is not sufficient that a patient with filariasis who has been in the tropics shows chronic superficial punctate keratitis or uveitis with eosinophilia; there must be proof of the presence of the exact species of the parasites in the eye. The presence of larvae of Onchocerca volvulus in the anterior chamber is not sufficient to produce an iritis. Allergic factors also seem to play a part in the origin of keratitis and uveitis. The only treatment known is the extirpation of the filarial nodules. This hinders the increase of embryos and prevents entry of larvae into the eye, as long as the carrier is guarded against new infection. The author recommends an application of 5 per cent mercurous chloride ointment in the conjunctival sac to alleviate keratitis punctata caused by filariasis in those cases which do not exhibit parasitic tumors.

Presse Médicale, Paris

55:693-708 (Oct. 18) 1947

*Preservation of Solutions of Penicillin and Streptomycin and of Combined Solutions of Penicillin and Streptomycin: Conclusions. G. Ramon and R. Richou.—p. 693.
*Bronchial Syndrome According to Bronchoscopic Observations. A. Soulas.—p. 694.
Considerations on Tracing of Syphilis by Systematic Serologic Examinations (Practical Value of Micromethods). M. Fourestier.—p. 695.

Preservation of Solutions of Penicillin and Streptomycin.—Experiments by Ramon and Richou demonstrated that penicillin treated with from 0.03 to 0.05 per cent of the commercial solution of formaldehyde for the solution of penicillin, or treated simultaneously with formaldehyde and warming up to 55 C. (131 F.), will retain its antibiotic properties and will not become contaminated with microbes for more than three months at temperatures of 2 to 4 C. (35.6 to 39.2 F.) and for four weeks at temperatures of 15 to 20 C. (59 to 68 F.). The same applies to solutions of streptomycin for a period of about four months at laboratory temperatures of 13 to 18 C. (55.4 to 64.4 F.) when 0.03 per cent of formaldehyde had been added to the solution of streptomycin. A combined solution of penicillin and streptomycin treated with formaldehyde will remain sterile and stable for a period of time comparable to that recorded for each of these substances in separate solution. The employment particularly of the combined solution will facilitate antibiotic therapy on a broader scale especially against mixed infections caused by bacteria partly resistant either to streptomycin or to penicillin or against infections in which the microbic agent has not been determined by laboratory methods before treatment is instituted. A combined solution of penicillin and streptomycin is indicated for local treatment of convalescents or carriers of diphtheria and for persons suffering from or exposed to whooping cough.

The Bronchial Syndrome.—According to Soulas the anatomophysiopathologic changes of the bronchial tube and of the bronchial wall have a controlling influence on the bronchial syndrome. Changes in the bronchial wall are characterized by edema, and that applies to transitory and superficial lesions resulting in functional disturbances, to organic lesions, such as erosive inflammation or ulceration, and to an involvement extending far below the surface, such as necrosis, stenosis or new growth. Whether superficial or deep, the parietal lesion produces disturbances lessening the secretion of mucus. There is also deficient expulsion of the bronchial secretion, due not only to the deficient vector represented by the cilia and the mucus but also to lessened motility of the wall. This threefold deficiency in the defense power of the bronchus causes not only obstruction but also stagnation and retention. Bronchoscopic treatment should be directed to the relief of the obstruction of the bronchial tree by clearing the bronchi and by restoring their secretory, excretory and motor power. The peribronchial tissue also plays an important part in the bronchial syndrome by representing the junction between the main bronchial tree and the parenchymatous area causing a response in one of the bronchoalveolar sectors. This relationship explains certain factors in extensive or localized pulmonary atelectasis in which the bronchial obstruction appears to be incomplete or there is only mild hypoventilation in spite of apparent complete obstruction. The same concept explains certain types of bronchiectasic suppuration which results from endobronchial and peribronchial lesions. It may also be an aid to understanding the localized so-called atelectatic or emphysematous processes temporarily associated with various bronchopulmonary disorders.

Book Notices

A Textbook of Medicine. Edited by Russell L. Cecil, A.B., M.D., Sc.D., Professor of Clinical Medicine, Cornell University Medical College, New York, with the assistance of Walsh McDermott, M.D., Associate Professor of Medicine, Cornell University Medical College. Associate Editor for Diseases of the Nervous System, Harold G. Wolff, M.D., Associate Professor of Neurology, Cornell University Medical College. Seventh edition. Cloth. Price, $12. Pp. 1730, with 244 illustrations. W. B. Saunders Company, West Washington Square, Philadelphia 5, 1947.

This latest edition of what has come to be a leading textbook of medicine is some 170 pages longer than the previous edition and has many revisions. Among the new articles in the current volume are many on nutritional disturbances, one on psychosomatic medicine and one on narcolepsy. Because of the deaths of some of the former contributors, new articles have been prepared on conditions caused by viruses, on many infections and on many disturbances of the nervous system. Some colored illustrations have been added to the text. Because of changes in knowledge of the etiology of certain diseases there are transpositions of material. Conspicuous is the resignation of Dr. Foster Kennedy as associate editor for diseases of the nervous system. His place has been taken by Dr. Harold G. Wolff, professor of medicine in charge of nervous diseases in the Cornell University Medical College. Because of the considerable number of specialists who contribute to this book and the careful editing, the volume continues to maintain a place of great importance among books available for teaching the practice of medicine.

Elementary Medical Physics. By Howard O. Stearns, Associate Professor of Physics, Simmons College, Boston. Cloth. Price, $4.75. Pp. 354, with illustrations. The Macmillan Co., 60 Fifth Ave., New York 11, 1947.

This textbook is written with the laudable idea of correlating the important subject of physics with biologic and medical sciences and of pointing out to the students where and how the laws of physics are applied to apparatus and instruments used in the practice of medicine. The objective of the author is meritorious. Too few textbooks on physics have been written for the premedical student, with the unfortunate result that in general the student has been less interested in physics than in any other basic science.

The book is aimed at the level of an introductory course in college. The author has made an attempt to simplify the mathematical analysis which is so necessary to an understanding of physics.

There are scattered through the book many applications of important laws and physical principles pertaining to biologic or medical sciences. This is an innovation, because many textbooks on physics employ mainly applications bearing on engineering or other technical uses. For example, to illustrate forces the bones and muscles of the body are depicted instead of a bridge or crane.

Colleges and universities training premedical students might well consider use of this textbook. It is recommended as a supplemental textbook for the special classes composed of premedical students only. Teachers of physical therapy and x-ray technicians will find the textbook a useful pedagogic aid.

The Fungi. Volumes I and II. By Frederick A. Wolf and Frederick T. Wolf. In two volumes. Cloth. Price, $6; $6.50. Pp. 438, with 153 illustrations; 538, with 82 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, 1947.

Fungi have received increased attention during recent years because of the important role that they play in many natural processes. These are specific processes such as (1) the production by fungi of penicillin and other antibiotics; (2) the use of fungi in many important fermentations, such as the manufacture of citric, fumaric, itaconic and other acids; (3) the role of fungi in the destruction of many kinds of service materials, including cotton and leather goods, optical instruments and electrical equipment, under tropical conditions, and (4) the causation by fungi of human diseases.

A great need exists for a comprehensive summary of present knowledge of the nature of fungi, their physiology and their role in natural processes. These two volumes have amply filled this need and serve as an introduction to more specialized fields.

The first volume is devoted to a discussion of isolation, cultivation and classification of fungi and a description of the more important groups.

Each chapter has adequate reference to literature wherein the reader can obtain further information. Each volume has a comprehensive author and subject index.

The chapter on medical mycology in the second volume will be of particular interest to the medical reader. After brief historical survey of the subject, the authors discuss important disease organisms such as Trichophyta or ringworm fungi, Coccidioides immitis, Histoplasma capsulatum, Aspergillus fumigatus, Sporotrichum schenckii, Actinomyces bovis and Monilia (candida).

Other chapters, notably those dealing with the poisonous and edible fungi and fungus-insect interrelationships, also are of definite interest. One would prefer inclusion of two additional chapters, one dealing with the production of antibiotics by fungi, and another on fungistatic and fungicidal agents.

The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine. Originally Written by William Osler, M.D., F.R.C.P. By Henry A. Christian, A.M., M.D., LL.D. Sixteenth edition. Cloth. Price, $10. Pp. 1539. D. Appleton-Century Co., Inc., 35 W. 32nd St., New York 1; 34 Bedford St., Strand London, W. C. 2, 1947.

Proof that time marches on is apparent in the sixteenth edition of Osler's "Principles and Practice of Medicine." The name Osler has disappeared from the cover, but the title page indicates that this is the book "originally written by William Osler, M.D."

Dr. Christian calls attention in his introduction to many additions that have been made since the last previous edition in 1944. These concern principally the use of the antibiotic and sulfonamide drugs in treatment and new classifications based on advancing knowledge of infections. "Catarrhal jaundice" and "Weil's disease" have been discarded, to be replaced by hepatitis of many varieties.

In this edition also appears a brief history of the Osler textbook of medicine prepared by Dr. James G. Carr of Chicago, with incidentally a facsimile of a note of appreciation written by William Osler in 1892. The present edition is approximately 40 pages longer than the last previous edition—an indication of the new material that has been added.

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Stop Annoying Your Children. By W. W. Bauer, M.D., Director, Bureau of Health Education, and Associate Editor of Hygeia. Cloth. Price, $2.75. Pp. 272, with illustrations. Bobbs-Merrill Co., 724-730 N. Meridian St., Indianapolis 7, 1947.

Even if the last chapter in this book had not been written by the author's daughter, it would have been obvious to the discerning reader that Dr. Bauer is a father. Only a sympathetic and understanding parent could have learned as much about child psychology as he evidently knows. The whole period of childhood, from infancy to adolescence, is covered in this little book, and virtually every problem that modern parents encounter is discussed in a clear, sensible manner. While Dr. Bauer's sympathy is with the child, he also has a kindly feeling for the parent.

Perhaps the motif of the book is expressed in this sentence: "The great difficulty which children face in making their decisions is lack of experience." Over and over Dr. Bauer makes the point that children must learn by the trial and error method and that parents make a mistake when they interfere too much with this method. The adult should not often attempt to force his opinions on the child, even though they are based on his own experience, but should rather present all sides of a question, then let the child decide for himself, or herself. "Nine chances out of ten," Dr. Bauer says, "she will make the correct decision."

Dr. Bauer's book will not flatter the ego of many—indeed, of most—parents, but it should make every parent who reads it without prejudice understand his children better. The author's smooth style and the delicious flavoring of humor in every chapter make the dose palatable, even though it is strong medicine. Furthermore, those conscientious parents who have been led to believe that a child's entire life can be ruined by a few mistakes made in the early years of inexperience will obtain

comfort from the chapter, "Turning Over a New Leaf." One sentence is especially comforting: "In spite of parental fears and in spite of parental blunders, most children do turn out all right."

Another comforting thought is to be found in the chapter, "Parents Can Be Wrong," in which the author says: "The capacity of our children for loyalty and forgiveness is almost unlimited. . . . It is a marvel that children have such a terrific loyalty to their parents."

Dr. Bauer's book can be commended unreservedly to young and even not-so-young parents who want to do right by their children. Its author might well have paraphrased Ambroise Paré's famous sentence: "See how I learned to treat gunshot wounds; not out of books." Dr. Bauer, although he gives a list of books on child psychology for reference, might well say of his own book: "See how I learned to deal with children; not out of books."

Atlas of Cardiovascular Diseases: Correlation of Clinical Electrocardiography and Cardiac Roentgenology with Clinical History and Autopsy Findings. By Irving J. Treiger, M.D., Assistant Professor of Medicine, University of Illinois, Chicago. Cloth. Price, $10. Pp. 180, with 69 plates. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1947.

The title page of this volume states that it is a "correlation of clinical electrocardiography and cardiac roentgenology with clinical history and autopsy findings." However, a careful study of the volume reveals many gaps in effective correlation. In the author's apparent endeavor to secure brevity he seems in a number of instances to have sacrificed clarity and effective discussion of the correlation of the observations. There are also several instances in which it is difficult to agree with his conclusions. One of the most striking examples is his statement that "correlation of history, physical findings, roentgenogram, and electrocardiogram leads to a correct understanding of the degree of anatomical and physiological changes in the heart and to a proper dose of various medications for their correction." One might agree, had the author said of a proper "selection" rather than "dose." Although in itself this is perhaps a minor misstatement, it could certainly prove highly misleading to the student or physician who was not too well acquainted with the subjects of pharmacology and therapeutics. This statement appears in the preface, but it is difficult, if not impossible, to find any elaboration of it in the context.

The illustrations are for the most part well executed, but unfortunately it is sometimes difficult to see in them the condition under discussion. For example, in plate 61 the legend mentions erosion of the thoracic vertebrae, but this condition is not revealed in the illustration.

Despite these shortcomings and others not specifically mentioned, the volume should prove useful to many as a source of graphic illustration chiefly of roentgenologic and anatomic observations in a fairly large range of cardiovascular diseases. In the hands of a competent teacher it might prove helpful as a basis for discussion of the various topics, the elaboration to be provided by the teacher.

However, when it is compared with some of the similar works on roentgenology of the heart and electrocardiography and their relation, it adds little of value to the existing literary armamentarium.

Dermatologic Clues to Internal Disease. By Howard T. Behrman, M.D., Assistant Clinical Professor of Dermatology, New York University College of Medicine, New York. Cloth. Price, $5. Pp. 165, with 118 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1947.

Those who favor small books with brief discussions in outline form will find this book to their liking. The material is arranged alphabetically. The descriptions of various symptoms and syndromes, intended to serve only as clues, are concise but adequate, and the illustrations in general are well selected. Many eponymic syndromes are described. The common skin diseases and the exanthems are omitted, and there is no bibliography. By the use of cross references and the avoidance of repetition, the author has successfully restricted the size of the book and fulfilled his objective to furnish a book of clues for the correlation of certain cutaneous symptoms and systemic diseases. Also, he has managed to include his own opinion on certain problems; it is not just a cold compilation of material.

Molding and Casting for Moulage Workers, Sculptors, Artists, Physicians, Dentists, Criminologists, Craftsmen, Pattern Makers and Architectural Modelers. By Carl Dame Clarke, Ph.D., Associate Professor of Art as Applied to Medicine, School of Medicine, University of Maryland, Baltimore. Second edition. Cloth. Price, $6.50. Pp. 300, with 99 illustrations. Standard Arts Press, 2635 N. Calvert St., Baltimore 18, 1946.

This is the second edition of "Molding and Casting." The present volume is larger than the first edition and its content of descriptive and illustrative matter has been considerably amplified.

The author explains the principles of technic in taking impressions and making casts. He describes fully the nature, behavior and method of manipulation of various types of materials used in these procedures. The use of plaster of paris molds, agar (hydrocolloid), gelatin, rubber and other substances is described, as are the various casting materials such as plaster of paris, wax and rubber.

While the book is of primary interest to medical artists specializing in plastic reproduction of anatomic and pathologic conditions, as well as in surgical procedures for making authentic records and for teaching purposes, it should find useful application in many other fields. Pathologists or anatomists who want to make their own preparations for use in classroom demonstration or lectures, preparators of museums of science and natural history and artists and craftsmen can all learn much from it.

This book should be useful to those interested in visual methods of instruction, particularly of a medical nature, as it explains the technic of preparing three-dimensional teaching aids, one of the most effective mediums of instruction. It gives numerous formulas for compounding material for taking impressions and making positive casts, which should mean considerable saving, provided that one has experience with such formulas.

One cannot help feeling that most of the chapter on "balsams, gums, resins, hydrocolloids and waxes" could have been left out, as a listing of such a large group of waxes, together with their physical and chemical properties, appears out of place in a book of this nature.

Since realistic appearance in most plastic reproductions of biologic specimens depends on fidelity of reproduction of color, in addition to reproduction of form, a more complete treatment of this all-important phase of the work would have improved the practical value of the book.

To the specialist the value of the book is naturally limited, but to the amateur it should prove a valuable guide.

Counseling in Schools of Nursing: A Study of the Principles and Techniques of Personnel Services for Students. By H. Phoebe Gordon, Assistant Professor of Nursing and Student Counselor, School of Nursing, University of Minnesota, Minneapolis; Katharine J. Densford, R.N., Professor of Nursing and Director, School of Nursing, University of Minnesota, and E. G. Williamson, Professor of Psychology and Dean of Students, University of Minnesota. Cloth. Price, $3. Pp. 279. McGraw-Hill Book Co., Inc., 330 W. 42d St., New York 18, 1947.

This book provides excellent orientation for administrators, counselors, instructors, supervisors, head nurses and general staff nurses in the problems of student nurses and the guidance which should be available to them. It should prove valuable in the preparation of the personnel specialist or counselor. The authors are particularly well qualified by training and experience to present the subject of counseling in an authoritative and comprehensive manner. Part 1 provides the historical background of nursing and personnel work, while 2 and 3 deal with the understanding of the student, her problems in nursing and types of counseling which are necessary. Part 4 offers a practical approach to organization and development of a personnel program.

The importance of good counseling to the student, who is enabled to make the most of her opportunities, is stressed throughout. The hospital and patient benefit by improved morale and better adjustment of the student. The hospital administrator or director of the school of nursing who questions the necessity of instituting a counseling program will find convincing evidence in this little volume of its economy in the functioning of the hospital nursing service and the nursing school.

This book received the First Award of the McGraw-Hill Book Awards in Nursing Education.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VENTILATION AND AIR BORNE INFECTIONS

To the Editor:—**Will good ventilation without drafts in a nursery in southern California decrease the transference of air borne infections? Please cite references on the effect of improved ventilation on the infection rate. I find no articles on the use of ventilation for the control of air pollution.** Irving J. King, M.D., Los Angeles.

ANSWER.—In moderate amounts, ventilation is efficient in reducing the number of micro-organisms in the air and perhaps the infant mortality also. Too much ventilation, such as is used where the air pollution is heavy, may do more harm than good by stirring up infected dust particles off the floor. Blackfan and his associates have shown that other physical factors, such as temperature, humidity and "housecleaning," are more important than ventilation in the incidence of infection in premature infants.

References:

Yaglou, C. P., and Wilson, U.: Disinfection of Air by Air Conditioning Processes, *Aerobiology*, A. A. A. S., p. 129, 1942.

Slot, G. A.: Effect of Decreased Ventilation on Infant Mortality and on Incidence of Diseases of Respiratory Tract in Adults, *Geneesk. tijdschr. v. Nederl.-Indië* **77**: 677 (March 16) 1937.

Blackfan, K. D., and others: The Premature Infant: A Study of the Effects of Atmospheric Conditions on Growth and on Development, *Am. J. Dis. Child.* **46**: 1175 (Nov.) 1933.

TWIN PREGNANCY AND PERIOD OF INSEMINATION AFTER OVULATION

To the Editor:—**I am interested in the possibility of the relationship of the occurrence of twin pregnancy and the period of insemination of the ovum after ovulation. I know of 1 case of twins in which coitus occurred on the nineteenth day of the menstrual cycle in a woman whose cycle averages twenty-eight days. Data from readers would be appreciated.** Hugh Macdonald, M.D., Peoria, Ill.

ANSWER.—There is suggestive evidence from comparative embryology that deleterious influences exerted on the fertilized egg may increase the incidence of twinning. However, in man there is no apparent relationship between the occurrence of multiple pregnancy and the period of insemination of the ovum after ovulation. There are considerable data which would indicate that ovulation usually occurs about fourteen days preceding the onset of the next menstrual period. This interval is rather constant regardless of the length of the menstrual cycles. The ovum is capable of being fertilized for a short period following ovulation, probably less than twenty-four hours.

Monozygotic twins represent early segmentation of the fertilized ovum. Dizygotic twins result from two separate ovulations and the fertilization of both ova. Two egg twinning is definitely influenced by heredity, parity and age.

EFFECT OF SPLENECTOMY ON THE BLOOD

To the Editor:—**A man sustained a fall in August 1946, rupturing the spleen and necessitating a splenectomy. He developed obstruction of the bowel twice following splenectomy, a pelvic abscess, collapse of the right lung and blood in the urine. He finally recovered. Blood examination after splenectomy revealed a leukocytosis of 46,000 gradually lowering to 13,000 at the present time with 59 per cent lymphocytes. There is 3 to 4 ounces retention of urine. Please give me the latest opinion on the effect of splenectomy on the blood. Does a high lymphocyte count cause extreme lassitude?** M.D., New York.

ANSWER.—Removal of the spleen is followed early by a mild anemia with the appearance of nucleated red cells, reticulocytes, polychromatophilia and Howell-Jolly bodies in the red cells and by leukocytosis and thrombocytosis. Some of these changes are thought to be evidence of an inhibitory effect of the spleen on bone marrow function. The anemia and thrombocytosis are transient, while in many cases there is a persistence of moderate leukocytosis with an increase in the lymphocytes and monocytes. Most patients have no symptoms following splenectomy, but some have been reported to have easy exhaustion and vague gastrointestinal complaints. There is no evidence of a relationship between mild lymphocytosis and lassitude.

PRESERVATION OF SKIN GRAFTS

To the Editor:—**I have in mind the possibility of preserving the life of a piece of skin accidentally cut off until granulation tissue has formed on the denuded area, at which time the skin would be grafted onto the area from which it came. I would appreciate information on this or related subjects or the name of some other source of rather complete information on this subject.** M.D., Minnesota.

ANSWER.—Skin grafts may be refrigerated under sterile conditions and successfully transplanted after a number of days. They should not be frozen. Usually there is no reason for doing this. About the only reason, during an elective operation, for doing a delayed graft would be if the patient's condition became such, after the grafts had been cut but before they were applied, to justify stopping the operation without application of the grafts; the grafts could then be refrigerated and applied later.

In the event of avulsed tissue, one would be much more sure of a take by applying the avulsed skin to the raw surface in the shortest period of time possible after the accident. Of necessity one frequently applies skin grafts to a granulating wound, but it is much to be preferred to apply grafts to a newly created wound rather than await granulations.

About the only preserved tissue commonly used with success for subcutaneous grafting is preserved cartilage.

HOME WATER SOFTENERS

To the Editor:—**In the July 1947 issue of *Consumers Research* an article by C. A. Tyler, Ph.D., on "Soft Water for the Home" says "If a softening system is installed, at least one tap (a cold water tap) should deliver water which has not been treated; water which has been softened should not be used for cooking or drinking." There is no further explanation. In your opinion, should softened water not be used for cooking or drinking?** A. J. Price, M.D., Canandaigua, N. Y.

ANSWER.—Home water softeners in their exchange of sodium for calcium in the dissolved salts in natural water may render the water less palatable, particularly if the "hardness" of the water is reduced to zero. A sudden change in the chemical characteristics of one's drinking water may cause some physiologic reaction.

The condition under which home water softeners are maintained and operated by persons inexperienced in water treatment may result in some contamination of the water.

For these reasons it may be desirable to install an additional cold water tap in the home. This does not mean however that in all cases softened water should not be used for drinking or cooking purposes. Public water supplies which are softened under technical supervision are usually so treated that both safety and palatability are assured and the supply is entirely potable.

PHLEBITIS

To the Editor:—**Please let me know the accepted treatment for edema of the lower extremity in these two cases: 1. A man with no history of phlebitis or clinical evidence of phlebitis has a few superficial varicosities and a dilated saphena magna. Is ligation of the saphena magna indicated? If so, what is the rationale for ligation? 2. A woman has had a ligation of the saphena magna, as evidenced by a scar in the groin; there is still evidence of a dilated saphena magna extending three fourths of the way up the thigh and also some superficial varicosities. What means, medical or surgical, would improve or cure edema of the extremity in this case? Pelvic examination is negative in both cases.** Alexander Zabin, M.D., Malverne, L. I., N. Y.

ANSWER.—1. Lack of history of phlebitis does not rule out deep venous obstruction or deep valvular insufficiency, since many patients develop segmental venous obstructions in the deep veins without obvious clinical symptoms. More important is the presence of deep venous obstruction or deep venous reflux. If the saphenous valve is demonstrably incompetent in the standing position, the ligation of the long saphenous vein at its junction with the femoral vein is reasonable, since it removes the back-pressure from above; however, if the saphenous dilatation is caused in addition by incompetent perforators, they may have to be interrupted either by multiple ligations or by stripping out the entire long saphenous vein. If the valvular incompetence is in the deep veins, operations or injections on the superficial venous system will never be of lasting benefit, since the increased deep venous pressure will produce additional varicosities through perforator channels. In such cases well fitting elastic hose may be prescribed; more recently some authors have advocated the division of the superficial femoral vein below the profunda with the idea of decreasing the deep venous pressure in the leg. Such operations can be done only by men specially interested in this field and only in cases in which the disadvantages of the deep venous reflux outweigh the disadvantages of deep venous obstruction. Generally speaking, serious ankle edema with dilatation

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of the saphenous system is more apt to be due to deep venous insufficiency, since uncomplicated saphenous varicosities seldom if ever produce ankle edema.

2. The presence of a dilated saphenous vein, in spite of a previous ligation, often means that the vein was insufficiently ligated and that the saphenous bulb is still patent with a number of tributaries. It is inadvisable for any one to ligate or inject such varicosities until he has satisfied himself as to the state of the superficial, communicating and deep valves. A pamphlet on varicose veins issued by the American Medical Association summarizes the necessary tests and the principles of treatment.

PROPHYLACTIC THERAPY IN PROLONGED LABOR

To the Editor:—**It is my impression that prophylactic therapy with penicillin and one of the sulfonamides is used as a routine procedure at the New York Lying-In Hospital in cases of ruptured membranes after twelve hours. This is based on extensive research by Dr. Douglas at that institution. Have you any information concerning this or any like procedure in any other leading clinic?**

Martin E. Tyrrell, M.D., Depew, N. Y.

ANSWER.—In cases of premature rupture of the membranes without labor it is usually not necessary to prescribe prophylactic penicillin and sulfadiazine therapy. Experience has indicated, however, that when the membranes rupture prematurely and a desultory labor ensues such treatment is of great value. It may at times be instituted early in labor, but it should always be started, if possible, before twenty-four hours of labor. Experience has indicated that, if we wait until intrapartum infection has actually developed, the employment of the drugs is not nearly so effective as when they are employed prophylactically. Accordingly, it is necessary to predict complications such as prolonged labor, difficult delivery and trial of labor. The incidence of both intrapartum infection and subsequent puerperal infection can be greatly reduced by such treatment. It has also been shown that if a cesarean section becomes necessary after a trial of labor it can be done with a great deal more safety if the prophylactic therapy has been given.

The usual dose of penicillin recommended is 20,000 units given intramuscularly at intervals of three hours. Under certain conditions this dosage may be increased for a short period to 50,000 units every two hours. The sulfonamide of choice is sulfadiazine, and an adequate dose usually consists of 1 Gm. every four hours with about four times that amount of sodium bicarbonate. Occasionally it is necessary to give the sulfadiazine intravenously, and under such circumstances it is best to administer it with, or following, 500 cc. sixth-molar lactate solution. Experience suggests that the indications for prophylactic therapy arise in about 10 per cent of patients.

RELIEF OF PAIN OF INOPERABLE CANCER

To the Editor:—**Please let me know the various accepted methods of relieving pain in inoperable cancer, especially carcinoma of the cervix, other than the use of narcotics.**

Alexander Zabin, M.D., Malverne, L. I., N. Y.

ANSWER.—Three surgical procedures are generally used to relieve intractable pain associated with inoperable carcinoma of the cervix: chordotomy, pelvic sympathectomy and intraspinal injection of alcohol. Chordotomy, which consists of section of the anterolateral spinal tracts, will relieve pain, but it is an operation which usually requires the skill of a neurosurgeon. Unless the incision in the cord is accurately placed, the pain may not be completely relieved or the motor pathway may be damaged, resulting in paralysis of the legs and interference with control of the sphincters. The technic of chordotomy is described by F. C. Grant (*Am. J. Obst. & Gynec.* **24**:620 [Oct.] 1932).

In pelvic sympathectomy the risk involved is slight, the technic is not complicated, and local infiltration anesthesia may be used for a large part of the operation. The type of operation usually performed is the one recommended by Cotté and consists in resection of the postganglionic fibers of the sympathetic nervous system which innervate the pelvic organs. The technic of pelvic sympathectomy is given by J. P. Greenhill and H. E. Schmitz (THE JOURNAL, July 1, 1933, p. 26).

Intraspinal injection of alcohol, which relieves pain by blocking the nerves that conduct pain sensation, is simple to carry out, entails very few risks and is highly effective in entirely or partially relieving pain associated with inoperable cancer of the cervix. The technic of intraspinal alcohol injection is given by E. L. Stern (*Am. J. Surg.* **25**:217 [Aug.] 1934) and by J. P. Greenhill, and H. E. Schmitz (THE JOURNAL, Aug. 10, 1935, p. 406).

SEQUELAE OF CONJUNCTIVITIS

To the Editor:—**A woman, a very intelligent nurse, aged 46, states that lid of her left eye is stuck to the cornea when she awakens. This has occurred fifty or sixty times in the last one and one-half years following a very bothersome conjunctivitis in both eyes. She keeps the membranes from sticking by the instillation of castor oil at night, the lids sticking in spite of this at times. When the lid and cornea are separated, there is discomfort, which disappears in about an hour. Examination is negative except for some superficial oval epithelium punctate markings at the lower margin of the left pupillary area. There seem to be a few of these in the right eye also. Her general health seems satisfactory. Her eyes are not subjectively dry, and a Schirmer test was normal.**

M.D., California.

[This inquiry was referred to two authorities, whose respective replies follow.—Editor.]

ANSWER.—Occasionally after an attack of keratoconjunctivitis the cornea may remain more or less insensitive for a long time. There is also in these cases a reduced lacrimal secretion, although the Schirmer test may not reveal this. If one adds to these conditions some faulty closure of the eyelids during sleep, the corneal epithelium becomes dry and sticks to the tarsal conjunctiva, producing the symptoms mentioned. Treatment consists in use of a cod liver oil ointment, with 5 per cent glucose mixed in, applied in the conjunctival sac before retiring, and the use of a "moist chamber" covering during sleep.

ANSWER.—This patient may have had an allergic conjunctivitis with a superficial punctate keratitis. Epithelial infiltrates are common findings in long standing conjunctival allergies. In such cases one drop of Lugol's solution in ½ ounce of 1 per cent potassium iodide, used three times a day, allows clearing in a few weeks. A boric acid ointment at night prevents discomfort on awakening in the morning.

PITYRIASIS OR TINEA VERSICOLOR

To the Editor:—**A woman aged about 30 consulted me three years ago with regard to a discoloration or pigmentation on the breasts about the size of a silver dollar which in a few weeks spread slowly to her shoulders. It is now down as far as the navel in front but only on the shoulders on the back and up the neck on the sides. It spreads slowly and in patches, some as large as my double hands and solid, and good skin is mingled with the pigmentation. The skin isn't raised and is smoother than normal skin but rather brown, and on some days red. It itches somewhat when she gets hot. It seems to scale off slightly and these particular spots feel dry. There is no pain. I first gave her Cofron Capsules, which didn't seem to help; then I gave her Thio-Bismol shots every other day for some time, then two each week. This was about two and a half years ago and it seemed to help some. During this time the discoloration was only on her shoulders. I thought she was getting along well and so stopped the shots. As time went on it got worse, so I gave more Thio-Bismol shots but didn't get as good results as at first. I took a blood test in 1942 and another in 1945 and both were negative. The temperature is 98.2 F., the blood pressure 112/60, the pulse rate 72. specific gravity of the urine 1,027, slightly acid, no sugar, and slight albuminuria. The teeth are in fair condition.**

M.D., Missouri.

ANSWER.—These pigmented spots, of various sizes and designs, with mild scaling probably are those of pityriasis or tinea versicolor. In this disorder there are slightly raised patches and sheets appearing on the flanks, usually not spreading through the midlines, and in extreme cases they may cover the entire torso. The patient develops a slight furfurescence or powdery scale which can be best appreciated by scraping the affected parts. At times the lesions are reddish, especially when they are irritated or after friction and sweating. There may be some itching. The lesions commence at the site of the follicles and then spread and coalesce with neighboring ones to form patches. This infection is said to occur in those who are given to much sweating and is commonly believed to occur more frequently for that reason perhaps in tuberculous subjects. This impression has not been verified by some observers. It is true, however, that some persons are subject to this disorder, and even though the apparent trouble is cleared, it tends to recur in them. The infection is due to a fungus called microsporon furfur, which lives on the surface of the skin and produces changes in the very superficial parts. The organism really should be classified as a saprophyte rather than one which produces any real pathologic condition. Treatment can be carried out simply with about 12 per cent sodium thiosulfate solution in water, sponged on the parts twice a day until they are cleared. Whatever the topical method used, it should be continued for an appreciable period after the lesions disappear. Other methods which have been employed with success are mercury bichloride water solution 1:5,000, a 3 to 5 per cent sulfur treatment and Whitfield's ointment (best carried out in ¼ to ½ strength).

This fungous infection has no effect on the general health and does not require any radical treatment. It tends to relapse. In those who are subject to it, simple treatment such as with the sodium thiosulfate solution may be continued twice a week after the lesions have cleared.

EXFOLIATIVE DERMATITIS

To the Editor:—A woman aged 20, with a history of rheumatic heart disease from childhood, developed symptoms of arthritis in March 1947. She was given a course of penicillin therapy amounting to about 1,500,000 units. In April several areas of redness and scaling on her body and seborrheic eczema of the scalp and ears developed. Subsequently exfoliative dermatitis involved the entire body. When first seen by me on June 19 the patient appeared extremely ill, with rapid pulse, temperature 102.6 F. and oozing from fissured areas in the folds of the body, with a profuse purulent discharge from both ears, swelling of the hands and feet and fissuring on the dorsal surface of the toes. After admission to the hospital her temperature dropped to normal within forty-eight hours. Culture of the ear discharge showed a pure growth of Proteus vulgaris. Urinalysis was negative. The blood counts ranged from 10,500 to 21,000 white blood corpuscles. The erythrocytes dropped from 3,750,000 to 2,750,000, and the hemoglobin from 68 per cent to 59 per cent. The differential count varied from 35 per cent to 3 per cent of polymorphonuclears. The lymphocytes ranged from 92 to 58 per cent. There was a slight shift to the left. Blood culture was negative. During the hospital stay all the fissures except those in the toe region were healed, but the exfoliation and the ear drainage continued. There is a considerable loss of hair. The lymph glands, liver and spleen were not enlarged. Is it possible that this condition could be a penicillin reaction or a preleukemic condition? I would appreciate any suggestion.

M.D., Florida.

ANSWER.—Skin eruptions following the use of penicillin are extremely variable. The commonest type of eruption following its use is urticaria, but maculopapular and erythematous lesions are not infrequent. Bullous lesions and exfoliative dermatitis have likewise been observed. The severe cases of exfoliative dermatitis that have been described rarely last more than three weeks. In the case under discussion, the nature of the onset of the eruption and its long duration, together with the profound changes in the blood, would make one question the diagnosis of penicillin sensitivity. The vast majority of eruptions appear within five to twenty-one days after penicillin is started and rarely persist more than twenty-one days after their appearance. Careful patch testing with penicillin might provide information concerning penicillin sensitivity.

APPLICATION OF SILVER NITRATE TO THE EYE

To the Editor:—My wife has been advised by an eye doctor to use silver nitrate. He himself applies it. It makes her quite uncomfortable. A member of the board of ophthalmology states that he has not used this in years. Please advise.

M.D., Alabama.

ANSWER.—Silver nitrate is extensively used for the prevention of ophthalmia neonatorum and in the treatment of mucopurulent conjunctivitis, trachoma, blepharitis and many other conjunctval inflammations. Its effect is due largely to a caustic action which coagulates superficial layers of the conjunctival epithelium, forming a bluish white eschar which is washed, wiped or cast off in flakes. Silver nitrate is not strongly antiseptic, but organisms are enmeshed in the coagulum and removed with it. A secondary effect arises from the irritation, which causes a hyperemia and flooding of the part with serum. The pain caused by application of the drug may be relieved by cocaine.

All silver salts are irritating to the eye, the degree of irritation paralleling the concentration of the drug used and to a great extent dependent on the nature of the salt used. Long continued use may result in the deposit of silver in the tissues (argyrosis), a condition which may rarely follow relatively few applications. Local application delays epithelization of the abraded cornea, and blindness has been known to follow the use of too strong a solution. Thus extreme care must be exercised whenever silver salts are used.

MONGOLIAN IDIOCY AND CRETINISM

To the Editor:—Are there any tests other than clinical examination to differentiate between mongolian idiocy and cretinism? How can one determine the basal metabolism of an 8 month old baby other than by direct calorimetry?

L. A. Crowell Jr., M.D., Lincolnton, N. C.

ANSWER.—It is usually possible to differentiate between mongolian idiocy and cretinism by the appearance of the patient. In occasional instances there may be some doubt as to the exact diagnosis and under these circumstances the two conditions can usually be differentiated by a therapeutic trial of desiccated thyroid. The initial dose for an 8 month old baby should be ¼ grain (15 mg.) of U. S. P. thyroid daily.

Direct calorimetry is carried out in only a few clinics in the country, and the results of basal metabolism determination in babies and very young children are open to question. In most instances in which the diagnosis is in doubt it is preferable to make a therapeutic test with desiccated thyroid rather than rely too much on basal metabolism determinations.

SEVERE BACK PAIN

To the Editor:—A veteran, 35, had his first severe episode of back pain while in Hollandia, New Guinea, and since then has had three recurrences of severe pain twice on the left side and once on the right side, typical of renal colic. Opiates relieved the pain. Red blood cells have appeared intermittently in the urine during and between the attacks. Two competent genitourinary surgeons have made thorough studies by cystoscopy, retrograde and intravenous pyelogram. No cause for the condition has been determined. Gallbladder, gastrointestinal x-rays and barium enema are negative. The blood count is normal. Stool examinations have been repeatedly negative. A centrifuge specimen of the urine on two occasions contained a small shiny red round object which we have been unable to identify. Is there a tropical disease endemic to New Guinea which could in some way be responsible for the occasional recurrences simulating renal colic?

M.D., New Jersey.

ANSWER.—Schistosomiasis is a tropical disease which could cause symptoms as outlined. Cystoscopically, schistosomiasis is characterized by small papillomatous and granulomatous lesions about the ureteral orifices. However, adnexal disease could also cause these symptoms. Vesiculitis in particular can cause hematuria and ureteral colic because of the proximity of the vesicle and ureter.

RETREATMENT OF SYPHILIS DURING PREGNANCY

To the Editor:—What is the best month for retreatment of syphilis during pregnancy? I have a patient who was treated for secondary syphilis in September 1946. She received 4,500,000 units of penicillin (50,000 units every three hours) as well as ten injections of oxophenarsine hydrochloride and four injections of bismuth subsalicylate in oil (1 cc. each). Her serum reaction, which was strongly positive at first, became negative in about six months and has continued so. At present she is going into her fourth month of pregnancy. I would appreciate knowing when retreatment should be started with penicillin and with what dosages; whether oxophenarsine hydrochloride and bismuth should also be given and whether a spinal tap should be taken and when. The husband has also been treated for the same condition and has likewise been negative since March.

M.D., Connecticut.

ANSWER.—It may be that the patient is cured and that there will be no danger of the fetus being infected. However, in view of the comparatively innocuous character of the remedy employed, we would recommend that in this particular situation the patient be given a daily intramuscular injection in alternating buttocks of penicillin calcium (peanut oil in beeswax) 300,000 units for a series of twelve injections. Moreover, the fourth month would be an ideal time to administer the treatment. In view of the almost specific effect of the drug in syphilis in pregnancy, no further treatment with heavy metal is necessary. A lumbar puncture is not recommended during pregnancy but should be done sometime after the birth of the baby. It would be well to continue the monthly titrated serologic test on both wife and husband until such a time as they have been completely negative for one year. Moreover, after delivery the child should likewise have a titrated serologic test beginning with the cord blood and at the second, fourth, sixth and twelfth month. It is only by the titered test that the true situation can be properly followed. A rise in the curve that persists and continues to increase indicates syphilis and imminent relapse.

TUBERCULOSIS AND WIND INSTRUMENTS

To the Editor:—Kindly advise me whether it is harmful to allow an adult patient with a healed pulmonary tuberculosis lesion to play a wind instrument.

M.D., New York.

ANSWER.—If the tuberculous lesion is completely healed, the answer is easy: in early or moderately advanced disease no particular harm can arise from blowing a wind instrument; if the disease was far advanced and the lung parenchyma over half destroyed, there would be a risk of producing or aggravating an emphysema, which practically always accompanies a far advanced healed disease.

Since few patients or physicians can always know whether complete healing has taken place in any given case, it is difficult to say just when such strenuous exercises can be begun even in early cases. A safe rule would be to have a negative stomach lavage for tubercle bacilli for at least two to three years after the usual clinical arrest of the disease.

PREGNANCY AND HODGKIN'S DISEASE

To the Editor:—Referring to a Query and Minor Note, "Pregnancy and Hodgkin's Disease," The Journal, Oct. 4, 1947, page 318, I submit the following reference: Kushner, J. Irving: Pregnancy Complicating Hodgkin's Disease (Lymphogranuloma Malignum), *Am. J. Obst. & Gynec.* 42:536-538 (Sept.) 1941, in which the history of a patient with pregnancy complicated by Hodgkin's disease is reported. This patient received radiation therapy during the early months of her pregnancy. A healthy child was born, whose subsequent development was normal.

J. Irving Kushner, M.D., New York.

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